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IN THE UNITED STATES RECEIVING OFFICE
Before the United States Receiving Office
for the Patent Cooperation Treaty

In re application of: Velpandi AYYAVOO; Thanadavarayan
NAGASHUNMUGAM and David B. WEINER

International Application No.: PCT/US98/19478

International Filing Date: 18 September 1998

Title: ATTENUATED VIF DNA IMMUNIZATION CASSETTES FOR GENETIC VACCINES

Assistant Commissioner for Patents
BOX PCT DO/EO/US
Washington, DC 20231

TRANSMITTAL LETTER SUBMITTING SEQUENCE LISTING

Applicant submits herewith the Sequence Listing in written (32 sheets) and computer readable form, the contents of which are the same.

The enclosed Sequence Listing does not go beyond the disclosure in the international application as filed.

Respectfully submitted,


Paul K. Legaard
Registration No. 38,534

/vc

Enc.: 1 Diskette; 32 sheets sequence listing
Date: 29 February 2000
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SEQUENCE LISTING

<110> Ayyavoo, Velpandi
Nagashunmugam, Thandavarayan
Weiner, David B.
University of Pennsylvania

<120> ATTENUATED VIF DNA IMMUNIZATION CASSETTES FOR GENETIC
VACCINES

<130> UPAP-0263

<140> HEREWITH

<141> 1998-09-18

<160> 46

<170> PatentIn Ver. 2.0

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Arg Ile Arg Thr Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Arg Trp Phe Tyr Arg His His Tyr Glu Ser Pro His Pro
35 40 45

Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu Glu
50 55 60

Thr Thr Thr Tyr Trp Gly Leu His Gly Glu Arg Asp Trp His Leu Gly
65 70 75 80

Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr Gln Val
85 90 95

Asp Pro Asp Leu Ala Asp Gin Leu Ile His Leu Tyr Tyr Phe Asp Cys
100 105 110

Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg Val Ser
115 120 125

Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser Leu Gln
130 135 140

Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro Pro
145 150 155 160

Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro Gln
165 170 175

Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 2

<211> 26

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<223> Description of Artificial Sequence: Novel Sequence

<400> 2

gaaagcttat gaaaaacaga tggcag 26

<210> 3

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<223> Description of Artificial Sequence: Novel Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Ser	Lys
	20						25				30				

Lys	Ala	Arg	Glu	Trp	Phe	Tyr	His	His	Tyr	Gln	Ser	Pro	His	Pro	Lys
	35				40					45					

Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu	Glu	Ile
	50				55				60						

Thr	Ser	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His	Leu	Gly
65				70				75			80				

Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr	His	Val
	85				90				95						

Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe	Asp	Cys
	100				105				110						

Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg	Val	Ser
	115				120				125						

Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser	Leu	Gln
	130				135				140						

Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	Pro	Pro
145						150			155			160			

Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys	Pro	Gln
	165				170					175					

Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His		
	180				185				190						

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5				10					15		

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
	35				40				45						

Pro	Arg	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50				55				60						

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65			70				75			80				

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Tyr	Ser	Thr
	85				90				95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130			135				140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145			150				155			160				

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
	165				170				175						

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
	180			185				190							

<210> 6

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5				10						15	

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
					20			25					30		

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
						35		40					45		

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
						50		55				60			

Glu	Thr	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
						65		70			75		80		

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
						85		90					95		

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
					100			105					110		

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115		120				125			

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
						130		135			140				

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
						145		150			155		160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165		170				175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185				190			

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<211> 192

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1					5				10					15	

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Thr	Tyr	His	Met	Tyr	Arg	Ser
					20				25				30		

Gln	Lys	Ala	Arg	Glu	Trp	Phe	Asn	Arg	His	His	Tyr	His	Ser	Pro	His
						35			40				45		

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
						50			55			60			

Ala	Ile	Pro	Thr	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
						65			70			75		80	

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
						85			90				95		

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
						100			105			110			

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115			120			125			

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
						130			135			140			

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
						145			150			155		160	

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180			185			190			

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10						15		

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
					20			25				30			

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
					35		40				45				

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
					50		55			60					

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
					65		70			75			80		

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
					85			90				95			

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	His	Leu	Ile	His	Leu	Cys	Tyr	Phe
					100		105			110					

Asp	Cys	Leu	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
					115		120			125					

Val	Ser	Pro	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser	
					130		135			140					

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
					145		150			155			160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170			175				

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
					180			185			190				

<210> 9

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<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
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Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
					20			25				30			

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
					35		40				45				

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
					50		55			60					

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65			70			75				80				

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
					85			90			95				

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
					100			105			110				

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
					115		120				125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
					130		135			140					

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145						150			155			160		

Pro	Pro	Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180			185			190			

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20						25					30			

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
	35					40					45				

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50					55			60						

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65					70			75			80			

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85						90					95			

Gin	Val	Asp	Pro	Asp	Leu	Ala	Asp	His	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100						105					110			

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115						120					125			

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130					135					140				

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145						150			155			160		

Pro	Pro	Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
							180		185			190			

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<212> PRT

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<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
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Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
35				40					45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
50				55				60							

Val	Ile	Thr	Thr	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
65				70				75			80				

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90					95					

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100			105				110							

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115			120				125							

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
130				135				140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145				150				155				160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
	165				170					175					

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
	180			185				190							

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<223> Description of Artificial Sequence: Novel Sequence

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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
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Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Asn	Arg	His	His	Tyr	His	Arg	Pro	His
	35					40			45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50				55			60							

Glu	Ile	Thr	Thr	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65				70			75		80					

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85					90			95						

Gin	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gin	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105			110							

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115					120			125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130				135			140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170			175				

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185		190					

<210> 13

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<212> PRT

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<223> Description of Artificial Sequence: Novel Sequence

<400> 13

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10					15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Gln	Lys	Glu	Arg	Glu	Trp	Phe	Asn	Arg	His	His	Tyr	His	Ser	Pro	His
	35				40				45						

Pro	Glu	Gln	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Val	Asp	Gly	Arg	Leu
	50				55				60						

Glu	Lys	Ile	Ala	Val	Trp	Ser	Leu	Asp	Thr	Gly	Glu	Gly	Val	Trp	His
	65				70			75		80					

Arg	Gly	His	Arg	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90				95						

Gln	Val	Asp	Pro	Asp	Leu	Val	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130				135				140						

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
	165				170				175						

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
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Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1					5				10				15		

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
					20			25				30			

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
					35		40				45				

Pro	Lys	Val	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Gly	Asp	Gly	Arg	Leu
					50		55			60					

Glu	Lys	Thr	Ala	Val	Trp	Ser	Leu	Gln	Ala	Gly	Asp	Gly	Val	Trp	His
					65		70		75			80			

Arg	Gly	His	Pro	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
					85			90				95			

Gln	Val	Asp	Pro	Asp	Leu	Val	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
					100		105			110					

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
						130		135			140				

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
						145		150		155			160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 15

<211> 191

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 15

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Arg Thr Trp Phe Ser Arg His His Tyr Gly Ser Pro His
35 40 45

Pro Lys Val Cys Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Ser Leu His Ala Gly Glu Asp Trp His Val
65 70 75 80

Gly Gln Arg Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr Gln
85 90 95

Val Asp Pro Asp Leu Ala Asp Gin Leu Ile His Leu Tyr Tyr Phe Asp
100 105 110

Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg Val
115 120 125

Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser Leu
130 135 140

Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro
145 150 155 160

Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro
165 170 175

Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 16

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 16

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5				10					15		

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Thr	Tyr	Phe	Ser
	20				25				30						

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40				45						

Pro	Asn	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55				60						

Val	Thr	Thr	Pro	Tyr	Trp	Gly	Leu	His	Gly	Gly	Glu	Arg	Asp	Trp	Tyr
65				70				75				80			

Leu	Ala	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
		85				90				95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130				135				140						

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145				150				155				160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165				170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 17

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met	Glu	Asn	Arg	Trp	Glu	Val	Met	Ile	Val	Trp	Glu	Val	Asp	Arg	Met
1				5			10					15			

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20				25				30						

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40				45						

Pro	Lys	Val	Ser	Ser	Glu	Va	l	Hi	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55				60							

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
	65			70			75			80					

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90				95						

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130			135				140							

Leu	Gin	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150				155			160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
	165				170				175						

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
	180			185				190							

<210> 18

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met	
1							5							10		15

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
							20					30			

Lys	Asn	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Asp	Ser	Pro	His
							35				40			45	

Pro	Val	Gln	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Gly	Asp	Gly	Arg	Leu
							50				55			60	

Gln	Lys	Ile	Ala	Phe	Trp	Ser	Leu	Asp	Ala	Gly	Glu	Arg	Asp	Trp	His
							65			70		75		80	

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
							85			90			95		

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
							100			105			110		

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
							115			120			125		

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
							130			135			140		

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
							145			150		155		160	

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
							165			170			175		

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Arg	His	Thr	Met	Asn	Gly	His
							180			185			190		

<210> 19

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 19

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5					10					15	

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20					25					30				

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Asp	Ser	Pro	His
	35				40				45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55				60						

Glu	Thr	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
65				70				75			80				

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85					90				95					

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gin	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130				135				140						

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145					150				155			160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165				170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185		190					

<210> 20

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 20

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10				15				

Thr	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
20					25				30						

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
35					40				45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
50					55			60							

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
65				70			75		80						

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
85					90				95						

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Thr	His	Leu	Tyr	Tyr	Phe
100					105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
115					120			125							

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
130				135				140							

Leu	Gin	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145					150				155			160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
165						170				175					

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
180					185				190						

<210> 21

<211> 188

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 21

Met	Glu	Asn	Arg	Trp	Gin	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10					15			

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
					20			25				30			

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Asn	Arg	His	His	Tyr	Asp	Arg	Pro	His
					35		40				45				

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
					50		55			60					

Glu	Ile	Thr	Thr	Phe	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
					65		70			75			80		

Leu	Gly	Gln	Arg	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
					85			90				95			

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Thr	His	Leu	Tyr	Tyr	Phe
					100		105			110					

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
					115		120			125					

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
					130		135			140					

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	
					145		150			155			160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170				175			

Pro	Gln	Lys	Thr	Lys	Gly	Thr	Glu	Gly	Ala	Ile	Gln				
					180			185							

<210> 22

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 22

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10				15				

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Phe	Val	Ser
	20				25				30						

Lys	Lys	Ala	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40			45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55			60							

Glu	Ile	Thr	Thr	Phe	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
	65			70			75		80						

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90				95						

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105			110							

Gly	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
	115				120			125							

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130				135			140							

Leu	Gln	Tyr	Leu	Gly	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170			175				

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185		190					

<210> 23

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 23

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5					10					15	

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
					20			25						30	

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
					35		40				45				

Pro	Gln	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
					50			55			60				

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
					65		70			75			80		

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
					85			90					95		

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
					100		105				110				

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
						130		135			140				

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	
						145		150			155			160	

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 24

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 24

Ile Glu Trp Arg Lys Lys Arg Tyr
1 5

<210> 25

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 25

Asp Arg Trp Asn Lys Pro Gln
1 5

<210> 26

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 26

Ser Leu Gln Tyr Leu Ala
1 5

<210> 27

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 27

atggaaaaca gatggcagggt gattatgtg tggcaggtag acagggatgg gattagaaca 60
tggAACAGTT tagtaaaata ccatatgtat tgatcaaaga aagctaggga atggTTTAT 120
tgacatcact atcaaAGTC tcattccaaa gtaagttag aagtacacat cccactagag 180
gatgtagat tggaaataac aacatatTTG ggtctgcata caggagaaag agactggcat 240
ttggTCAGG gagtctccat agaatggagg aaaaggagat atagcacaca cgtcgaccct 300
gatctAGCAG accaactaT tcactgtat tattttgat gttttcaga atctgtata 360
agaaaaGCCA tattaggaca cagagttagt cctaggTTG aatatcgagc aggacatagc 420
aaggtagat cactacGTA ctggcaata gcagcataa taacacaaa aaagataaag 480
ccacCTTGC cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggGCCACA gaggggGCCA tacaatgaat ggacactag 579

<210> 28

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 28

atggaaaaca gatggcagggt gatgtatTTG tggcaggtag acaggatgg gattagaaca 60
tggAACAGTT tagtaaaata ccatatgtat agatcaaaga aagctaggga atggTTTAT 120
agacatcact atcaaAGTC tcattccaga gtaagttag aagtacacat cccactagag 180
gatgtagat tggaaataac aacatatTTG ggtctgcata caggagaaag agactggcat 240
ttggTCAGG gagtctccat agaatggagg aaaaggagat atagcacaca ctagaccct 300
gatctAGCAG accaactaT tcactgtat tattttgat gttttcaga atctgtata 360
agaaaaGCCA tattaggaca cagagttagt cctaggTTG aatatcgagc aggacatagc 420
aaggtagat cactacGTA ctggcaata gcagcataa taacacaaa aaagataaag 480
ccacCTTGC cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggGCCACA gaggggGCCA tacaatgaat ggacactag 579

<210> 29

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 29

atggaaaaca gatggcagggt gatgtatTTG tggcaggtag acaggatgg gattagaaca 60
tggAACAGTT tagtaaaata ccatatgtat agatcaaaga aagctaggga atggTTTAT 120
agacatcact atcaaAGTC tcattccaaa gtaagttag aagtacacat cccactagag 180
gatgtagat tggaaataac aacatatTTG ggtctgcata caggagaaag agactggcat 240
ttggTCAGG gagtctccat agaatggagg aaaaggagat atagcacaca ctagaccct 300

gatcttagcag accaactaat tcacatgtat tattttgatt gttttcaga atctgcata 360
agaaaagcca tattaggaca cagagttagt cctagggttg aatatcgacg aggacatagc 420
aggtaggat cactacagta ctggcaata gcagcattaa taacacaaaa aaagataaa 480
ccacctttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggcccaca gaggagcca tacaatgaat ggacatag 579

<210> 30

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 30

atggaaaaca gatggcagggt gatgtatgt tgccaggtagt acaggatggat gattagaaca 60
tggAACAGTT tagtaacata ccatatgtat agatcacaga aagctaggaa atggtttaat 120
agacatcaat atcacatgtcc tcatccaaaa gtaatgtcag aagtccacat cccactagag 180
gatgtatgtat tgccaaatacc aacattttgg ggtctgcata caggagaag agactggcat 240
ttgggtcagg gagtctccat agaatggagg aaaaggatag atagcacacaa agtagaccc 300
gatcttagcag accaactaat tcacatgtat tattttgatt gttttcaga atctgcata 360
agaaaagcca tattaggaca cagagttagt cctagggttg aatatcgacg aggacatagc 420
aggtaggat cactacagta ctggcaata gcagcattaa taacacaaaa aaagataaa 480
ccacctttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggcccaca gaggagcca tacaatgaat ggacatag 579

<210> 31

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 31

atggaaaaca gatggcagggt gatgtatgt tgccaggtagt acaggatggat gattagaaca 60
tggAACAGTT tagtaaaaata ccatatgtat agatcaaaga aagctaggaa atggttttat 120
agacatcaat atcaaagtcc tcatccaaaa gtaatgtcag aagtccacat cccactagag 180
gatgtatgtat tgccaaatacc aacatattgg ggtctgcata caggagaag agactggcat 240
ttgggtcagg gagtctccat agaatggagg aaaaggatag atagcacacaa cgtcgaccc 300
gatctcgacg accaactaat tcacatgtat tattttgatt gttttcaga atctgcata 360
agaaaagcca tattaggaca cagagttagt cctagggttg aatatcgacg aggacatagc 420
aggtaggat cactacagta ctggcaata gcagcattaa taacacaaaa aaagataaa 480
ccacctttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggcccaca gaggagcca tacaatgaat ggacatag 579

<210> 32

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 32

atggaaaaca gatggcaggt gatgattgtg tggcaggttag acaggatgag gattagaaca 60
tggaaacagt tagtaaaaaa ccatacgat agatcaaaga aagcttaggg 120
agacatcaact atcaaaggcc tcattaaaaa gtaatttcg aagtacacat cccactagag 180
gtatcgat tggtaataac aacatatgg ggctcgata caggagaaaag agactggcat 240
ttggtcagg gagtctccat agaatggagg aaaaggagat atagcacaca ctagaccc 300
gatctagcag accaactaat tcacatgtat tattttgat gttttcaga atctgcata 360
agaaaaaggca tattaggaca caggtttagt cttaggttg aatatcgacg aggacatagc 420
aaggtaggat caactacgat ctggcaata gcacattaa taacaccaaa aaagataaag 480
ccacccttgc cgagtgtcga gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggggacca tacaatgaat ggacactag 579

<210> 33

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 33

atggaaaaca gatggcaggt gatgattgtg tggcaggttag acaggatgag gattagaaca 60
tggaaacagt tagtaaaaaa ccatacgat agatcaaaga aagcttaggg 120
agacatcaact atcaaaggcc tcattaaaaa gtaatttcg aagtacacat cccactagag 180
gtatcgat tggtaataac aacatatgg ggctcgata caggagaaaag agactggcat 240
ttggtcagg gagtctccat agaatggagg aaaaggagat atagcacaca ctagaccc 300
gatctagcag accaactaat tcacatgtat tattttgat gttttcaga atctgcata 360
agaaaaaggca tattaggaca caggtttagt cttaggttg aatatcgacg aggacatagc 420
aaggtaggat caactacgat ctggcaata gcacattaa taacaccaaa aaagataaag 480
ccacccttgc cgagtgtcga gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggggacca tacaatgaat ggacactag 579

<210> 34

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 34

atggaaaaca gatggcaggt gatgattgtg tggcaggtac acaggatgag gattagaaca 60
tggaaacagt tagtaaaaata ccatacgat agatcaaaga aactcgaggaa atggttttat 120
agacatcact atccaaatgc tcatccccaaa gtaagttcag aagtacacat cccactagag 180
gatgctagat tggttaataac aacattttgg ggtctgcata caggagaag agactggcat 240
ttgggtcagg gagttccat agaatggagg aaaaggagat atagcacaca ctgtgaccct 300
gatcttagcag accaactaat tcacatgtat tattttgatt gtttttcaga atctgcata 360
agaaaaagcca tattaggaca cagagttagt cctagggttg aatatcgagc aggacatagc 420
aaggtagat cactacatgat ctggcaata cgacgattaa taacccaaa aaagataaag 480
ccacccttgc cgagttgcag gaaatgcaca gaggatgat ggaacaagcc ccagaagacc 540
aagggtcaca gaggggcca tacaatgaat ggacactag 579

<210> 35

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 35

atggaaaaca gatggcaggt gatgattgtg tggcaggtac acaggatgag gattagaaca 60
tggaaacagt tagtaaaaata ccatacgat agatcaaaga aactcgaggaa atggttttat 120
agacatcact atccacccgtcc tcatccccaaa gtaagttcag aagtccacat cccactagag 180
gatgctagat tggttaataac aacattttgg ggtctgcata caggagaag agactggcat 240
ttgggtcagg gagttccat agaatggagg aaaaggagat atagcacaca agtagaccct 300
gatcttagcag accaactaat tcacatgtat tattttgatt gtttttcaga atctgcata 360
agaaaaagcca tattaggaca cagagttagt cctagggttg aatatcgagc aggacatagc 420
aaggtagat cactacatgat ctggcaata cgacgattaa taacccaaa aaagataaag 480
ccacccttgc cgagttgcag gaaatgcaca gaggatgat ggaacaagcc ccagaagacc 540
aagggtcaca gaggggcca tacaatgaat ggacactag 579

<210> 36

<211> 584

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 36

atggaaaaca gatggcaggt gatgattgtg tggcaggtac acaggatgag gattagaaca 60

tggaaacgtt tagtaaaaata ccatatgtat tgcataaaga aaagaagaagaa agggaaatgtt 120
 ttatagaca tcactatcac agccctcac cagaacaaag tcaacagcc cacatccgc 180
 tagtggatgg tagattggaa aaaaatgcgat tttggatctt ggatcaggaa gatggcgctt 240
 ggcacagggg gcatcgagtc tccatagaat ggagaaaaag gagatatgc acacaatgtt 300
 accctgtat agtagacaa ctaatcatac tgatatttt tgatgtttt tcagaatctg 360
 ctataaaaaa agccatatta ggacacagag ttatgcctag gtgtgaatat cgagcaggac 420
 atagcaagggtt aggtacata cagtagttt caatagcgc attataaca ccaaaaaaga 480
 taaggccacc ttggccagtgtcaggaaac tgacagagga tagatggaaac aagccccaga 540
 agaccaaggg ccacagaggg agccatacaa tgaatggaca ctat 584

<210> 37

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 37

atggaaaaaca gatggcaggt gatgttttg tggcaagtag acaggatgag gattagaaca 60
 tggaaacgtt tagtaaaaaca ccatatgtat ttgcataaaga aagctaaagaa aaggttttat 120
 agacatcaact atggaaagccc tcataaaaaa gtatgtcaaa cagccccat cccgctagg 180
 gatgtttagat ttggaaaaac agcgtttttt agtctgcagg caggagatgg agtctggcac 240
 agggggccatc cagtcctcat agaatggggg aaaaggagat atagcacaca agtagaccct 300
 gatgtttagat accaactaat tcatctgtat tattttgatt ttgtttcaga atctgtatata 360
 agaaaaaggcca tatttagata tagatgttgc ttctatgtttt aatccaaagc aggacataat 420
 aaggtagat ctctacatgtt ctggcacta cggccattaa taacccaaa gaagatataag 480
 ccaccttgc ctatgttgc gaaactgcata gaggatagat ggaacaagcc ccagaagacc 540
 aagggccaca gaggggccca tacaatgtat ggacactat 579

<210> 38

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 38

atggaaaaaca gatggcaggt gatgttttg tggcaagtag acaggatgag gattagacca 60
 tggaaacgtt tagtaaaaaca ccatatgtat ttgcataaaga aagctggac atggttttat 120
 agacatcaact atggaaagccc tcataaaaaa gtatgttcag aagtacacat cccactagg 180
 gatgtttagat ttgggtataac aacatattttt agtctgcagg caggagaatgg agactggcac 240
 ttgggtcaga gaggatctcat agaatggggg aaaaggagat atagcacaca agtagaccct 300
 gacttggcag accaactaat tcacatgtat tattttgatt ttgtttcaga atctgtatata 360

agaaaaagcca tattaggata tagagttgt cttaggttgt aataccaagc aggacataat 420
aaggtaggat ctctacagta ctggcacta gcagcattaa taacaccaa gaagataaag 480
ccacccitgc ctatgttgtg gaaatcgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggggagcca tacaatgaat ggacactag 579

<210> 39

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 39

atggaaaaca gatggcaggt gatgattgtg tggcaagtag acaggatgag gattagagca 60
tggaaacagt tagtaaaaaca ccatatgtat tttaaaga aagctaagaa atggttttat 120
agacatcaact atgaaaagccc tcaticaaaa gtaagtctag aagtacacat cccactaggg 180
gtatgtatgt tggtgacaaac accatattgg ggtctgcatg gaggagaaag agactggat 240
ctggcgcagg gagtcctcat agaatggagg aaaaggagat atagcacaca atgacccct 300
gaccctggcag accaactaat tcacitgtat tttttgtt gttttcaga atctgtata 360
agaanagcca tattaggata tagagttgt cttaggttgt aataccaagc aggacataat 420
aaggtaggat ctctacagta ctggcacta gcagcattaa taacaccaa gaagataaag 480
ccacccitgc ctatgttgtg gaaatcgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggggagcca tacaatgaat ggacactag 579

<210> 40

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 40

atggaaaaca gatgggaggt gatgattgtg tgggaagtag acaggatgag gattagagca 60
tggaaacagt tagtaaaaaca ccatatgtat tttaaaga aagctaagaa atggttttat 120
agacatcaact atgaaaagccc tcaticaaaa gtaagtctag aagtacacat cccactaggg 180
gtatgtatgt tggtgataac accatattgg ggtctgcatg caggagaaag agactggat 240
ttgggtcagg gagtcctcat agaatggagg aaaaggagat atagcacaca atgacccct 300
gaccctggcag accaactaat tcacitgtat tttttgtt gttttcaga atctgtata 360
agaanagcca tattaggata tagagttgt cttaggttgt aataccaagc aggacataat 420
aaggtaggat ctctacagta ctggcacta gcagcattaa taacaccaa gaagataaag 480
ccacccitgc ctatgttgtg gaaatcgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggggagcca tacaatgaat ggacactag 579

<210> 41

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 41

atggaaaaaca gatggcaggt gatgttgtg tggcaagtag acaggatgag gattagagca 60
tggaaacagt tagtaaaaaca ccatatgtat gttccaaagaac acgctaaagaa atggtttat 120
cgacatcaact atgacagccc tcataccatgc caaatgtcaa cagccccat cccgctaggg 180
gtatgtatgt tgccaaaaat acgtttttgg agtcttgatg caggagaaaag agactggcat 240
ttgggttcagg gagtctccat agatggagg aaaaggatag atagcacaca atgacacct 300
gaccctggcag accaaactaat tcatacgtat tttttgtt gttttcaga atctgtata 360
agaaaaaggcca tattaggata tagatgtt cttaggttgtt aataccaaagc aggacataat 420
aaggtaggt ctctacatgtt ctggcacta gcagcatataa taacacccaa gaagataaag 480
ccaccctttc ctatgttgtg gagaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggggcaca gaggggggca tacaatgtt ggacactag

579

<210> 42

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 42

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tggaaacagt tagtaaaaaca ccatatgtat gttccaaagaac acgctaaagaa atggtttat 120
agacatcaact atgacagccc tcataccaaaa gtaatgtca gaaatcacat cccacttaggg 180
gtatgtatgt tgccatataac acatattttgg ggtcttgatg caggagaaaag agactggcat 240
ttgggttcagg gagtctccat agatggagg aaaaggatag atagcacaca atgacacct 300
gaccctggcag accaaactaat tcatacgtat tttttgtt gttttcaga atctgtata 360
agaaaaaggcca tattaggata tagatgtt cttaggttgtt aataccaaagc aggacataat 420
aaggtaggt ctctacatgtt ctggcacta gcagcatataa taacacccaa gaagataaag 480
ccaccctttc ctatgttgtg gagaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggggcaca gaggggggca tacaatgtt ggacactag

579

<210> 43

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 43

atggaaaaca gatggcagg t gatgattgt tggcaagtag acaggatgac gattagagca 60
tggaaacagg tt tagaaaaaca ccatatgtat gtttcaaaga a a g c t a a g a a t g g t t t t a t 120
a g a c a t c a c t a t g a a a g c c c t a t c c a a a a g t a a g t t c a g a g t a c a c a t c c a c t a g g g 180
gatgctagat tggtgataac aacatattgg ggtcgc a g a g t a c a c a t c c a t a g g g 240
ttgggtcagg g a g t c t c c a t a g a a t g g a g g a g a t a g c a c a c a a g t a g a c c t 300
gacttgcagg accaactaac tcactgtat tattttgatt gttttcaga atcigctata 360
a g a a a g c c a t t a g g a t t a g a g t t g a t c t a g g t t g a t a f a t c a a g c a g g a c a t a a t 420
a a g g t t g a g t c t c a c a g t a c t g g c a c t a g c a g t t a a c a c c a a a g a a g a t t a a a g 480
c c a c t t t g c c t a g t g t g a g a a c t g a c a g a g g a t a g g a t a g g a a g c c c c a g a a g a c c 540
a a g g g c a c a g a g g a g c c a t a c a t g a t g a c a t g a t g a c a t g a t g a c a t g a t 579

<210> 44

<211> 578

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 44

atggaaaaca gatggcagg t gatgattgt tggcaagtag acaggatgag gattagagca 60
tggaaacagg tt tagaaaaaca ccatatgtat gtttcaaaga a a g c t a a g a a t g g t t t t a t 120
a g a c a t c a c t a t g a a a g c c c t a t c c a a a a g t a a g t t c a g a g t a c a c a t c c a t a g g g 180
gatgctagat tggagataac aacattttg ggtcgc a g a g t a c a c a t c c a t a g g g 240
ttgggtcagg g a g t c t c c a t a g a a t g g a g g a g a t a g c a c a c a a g t a g a c c t 300
gacttgcagg accaactaac tcactgtat tattttgatt gttttcaga atcigctata 360
a g a a a g c c a t t a g g a t t a g a g t t g a t c t a g g t t g a t a f a t c a a g c a g g a c a t a a t 420
a a g g t t g a g t c t c a c a g t a c t g g c a c t a g c a g t t a a c a c c a a a g a a g a t t a a a g 480
c c a c t t t g c c t a g t g t g a g a a c t g a c a g a g g a t a g g a t a g g a a g c c c c a g a a g a c c 540
a a g g g c a c a g a g g a g c c a t a c a t g a t g a c a t g a t g a c a t g a t g a c a t g a t 578

<210> 45

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 45

atggaaaaca gatggcagg t gatgattgt tggcaagtag acaggatgag gattagagca 60

tggacagtt tagaaaaca ccataatgtt ttttcaaga aagctaagaa atggttttat 120
agacatcaat atgaaaggcc tcataccaaa gtaagttcg aagtacacat cccactaggg 180
tgatctatggat tgagatcaa aacattttgg ggctcgtcg caggagaag agactggcat 240
ttgggtcagg gagtctccat agaatgggg aaaaggat atagcacaca atgtagaccct 300
gaccttgcag accaactaat tcatctgtat tatttttgtt tttttcaga atctgtata 360
agaaaaagcca tattaggata tagagttgtt ccttagttgt aataccaagc aggacataat 420
aaggtagat ctctacagta ctgggacta gcagcattaa taacacccaa gaagataaag 480
ccacccttgc ctatgttgag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggcccaca gaggagccca tacaatgaat ggacactag 579

<210> 46

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 46

atggaaaaca gatggcaggat gatgattgtg tggcaagtag acaggatgg gatttagagca 60
tggAACAGTT tagaaaaca ccataatgtt ttttcaaga aagctaagaa atggttttat 120
agacatcaat atgaaaggcc tcataccaaa gtaagttcg aagtacacat cccactaggg 180
tgatctatggat tgagatcaa aacattttgg ggctcgtcg caggagaag agactggcat 240
ttgggtcagg gagtctccat agaatgggg aaaaggat atagcacaca atgtagaccct 300
gaccttgcag accaactaat tcatctgtat tatttttgtt tttttcaga atctgtata 360
agaaaaagcca tattaggata tagagttgtt ccttagttgt aataccaagc aggacataat 420
aaggtagat ctctacagta ctgggacta gcagcattaa taacacccaa gaagataaag 480
ccacccttgc ctatgttgag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggcccaca gaggagccca tacaatgaat ggacactag 579

SEQUENCE LISTING

<110> Ayyavoo, Velpandi
Nagashumugam, Thandavarayan
Weiner, David B.
University of Pennsylvania

<120> ATTENUATED VIF DNA IMMUNIZATION CASSETTES FOR GENETIC
VACCINES

<130> UPAP-0263

<140> HEREWITH

<141> 1998-09-18

<160> 46

<170> PatentIn Ver. 2.0

<210> 1

<211> 190

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 1

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Arg Trp Phe Tyr Arg His His Tyr Glu Ser Pro His Pro
35 40 45

Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu Glu
50 55 60

Thr Thr Thr Tyr Trp Gly Leu His Gly Glu Arg Asp Trp His Leu Gly
65 70 75 80

Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr Gln Val
85 90 95

Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe Asp Cys
100 105 110

Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg Val Ser
115 120 125

Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser Leu Gln
130 135 140

Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro Pro
145 150 155 160

Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro Gln
165 170 175

Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 2

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 2

gaaagcttat ggaaaacaga tggcag 26

<210> 3

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 3

gcaaaggctt cattgtatgg ctc 23

<210> 4

<211> 190

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 4

Met Glu Asn Arg Trp Gln Val Ile Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Ser Lys
20 25 30

Lys Ala Arg Glu Trp Phe Tyr His His Tyr Gln Ser Pro His Pro Lys
35 40 45

Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu Glu Ile
50 55 60

Thr Ser Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His Leu Gly
65 70 75 80

Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr His Val
85 90 95

Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe Asp Cys
100 105 110

Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg Val Ser
115 120 125

Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser Leu Gln
130 135 140

Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro Pro
145 150 155 160

Leu Ala Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro Gln
165 170 175

Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 5

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 5

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gln Ser Pro His
35 40 45

Pro Arg Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Tyr Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 6

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 6

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gln Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Glu Thr Thr Thr Tyr Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 7

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 7

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Thr Tyr His Met Tyr Arg Ser
20 25 30

Gln Lys Ala Arg Glu Trp Phe Asn Arg His His Tyr His Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Ala Ile Pro Thr Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 8

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 8

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gln Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Tyr Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp His Leu Ile His Leu Cys Tyr Phe
100 105 110

Asp Cys Leu Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 9

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 9

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gin Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Ala Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 10

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 10

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gln Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp His Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Ala Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 11

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 11

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gin Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 12
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 12
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Asn Arg His His Tyr His Arg Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 13
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 13
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Gln Lys Glu Arg Glu Trp Phe Asn Arg His His Tyr His Ser Pro His
35 40 45

Pro Glu Gln Ser Ser Thr Ala His Ile Pro Leu Val Asp Gly Arg Leu
50 55 60

Glu Lys Ile Ala Val Trp Ser Leu Asp Thr Gly Glu Gly Val Trp His
65 70 75 80

Arg Gly His Arg Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Val Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 14

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 14

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Lys Val Ser Ser Thr Ala His Ile Pro Leu Gly Asp Gly Arg Leu
50 55 60

Glu Lys Thr Ala Val Trp Ser Leu Gln Ala Gly Asp Gly Val Trp His
65 70 75 80

Arg Gly His Pro Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Val Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 15
<211> 191
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 15
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Arg Thr Trp Phe Ser Arg His His Tyr Gly Ser Pro His
35 40 45

Pro Lys Val Cys Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Ser Leu His Ala Gly Glu Asp Trp His Val
65 70 75 80

Gly Gln Arg Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr Gln
85 90 95

Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe Asp
100 105 110

Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg Val
115 120 125

Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser Leu
130 135 140

Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro
145 150 155 160

Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro
165 170 175

Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 16
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 16
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Thr Tyr Phe Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Asn Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Val Thr Thr Pro Tyr Trp Gly Leu His Gly Gly Glu Arg Asp Trp Tyr
65 70 75 80

Leu Ala Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 17

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met Glu Asn Arg Trp Glu Val Met Ile Val Trp Glu Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 18

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Asn Ala Lys Lys Trp Phe Tyr Arg His His Tyr Asp Ser Pro His
35 40 45

Pro Val Gln Ser Ser Thr Ala His Ile Pro Leu Gly Asp Gly Arg Leu
50 55 60

Gln Lys Ile Ala Phe Trp Ser Leu Asp Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Arg His Thr Met Asn Gly His
180 185 190

<210> 19
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 19
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Asp Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Thr Thr Thr Tyr Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 20

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 20

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Thr Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Tyr Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Thr His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 21

<211> 188

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 21

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Asn Arg His His Tyr Asp Arg Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Phe Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Arg Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Thr His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gin Lys Thr Lys Gly Thr Glu Gly Ala Ile Gln
180 185

<210> 22

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 22

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Phe Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Phe Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Gly Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Gly Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 23

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 23

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Glu Ser Pro His
35 40 45

Pro Gln Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Tyr Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 24

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 24

Ile Glu Trp Arg Lys Lys Arg Tyr
1 5

<210> 25

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 25

Asp Arg Trp Asn Lys Pro Gln
1 5

<210> 26

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 26

Ser Leu Gln Tyr Leu Ala
1 5

<210> 27

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 27

atggaaaaca gatggcagg tggatgtg tggcaggtacaggatgag gattagaaca 60
tggacagt tagtaaaaatccatgtat tgatcaaga aagctaggaa atggtttat 120
tgacatcat atcaaagtcc tcatccaaa gtaagtcag aagtacacat cccactagag 180
gatgttagat tggaaataaac atcatattgg ggtctgcata caggagaaag agactggcat 240
ttggtcagg gagtcctcat agaaftggagg aaaaggagat atagcacaca ctgcgaccct 300
gatctcgac accaactaat tcacatgtat tattttgatt gttttcaga atctgcata 360
agaaaaagcca tattggaca cagagttgt cctaggttg aatatcgac aggacatagc 420
aaggttagat cactacagta ctggcaata cgacattaa taacacaaa aaagataaag 480
ccacccattttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggagccatacaatgaat ggacactag 579

<210> 28

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<210> 28

atggaaaaca gatggcagg tggatgtg tggcaggtacaggatgag gattagaaca 60
tggacagt tagtaaaaatccatgtat agatcaaga aagctaggaa atggtttat 120
agacatcat atcaaagtcc tcatccaaa gtaagtcag aagtacacat cccactagag 180
gatgttagat tggaaataaac aacatattgg ggtctgcata caggagaaag agactggcat 240
ttggtcagg gagtcctcat agaaftggagg aaaaggagat atagcacaca agtagaccct 300
gatctcgac accaactaat tcacatgtat tattttgatt gttttcaga atctgcata 360
agaaaaagcca tattggaca cagagttgt cctaggttg aatatcgac aggacatagc 420
aaggttagat cactacagta ctggcaata cgacattaa taacacaaa aaagataaag 480
ccacccattttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggagccatacaatgaat ggacactag 579

<210> 29

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<210> 29

atggaaaaca gatggcagg tggatgtg tggcaggtacaggatgag gattagaaca 60
tggacagt tagtaaaaatccatgtat agatcaaga aagctaggaa atggtttat 120
agacatcat atcaaagtcc tcatccaaa gtaagtcag aagtacacat cccactagag 180
gatgttagat tggaaataaac aacatattgg ggtctgcata caggagaaag agactggcat 240
ttggtcagg gagtcctcat agaaftggagg aaaaggagat atagcacaca agtagaccct 300

gatctagcag accaactaat tcatctgtat tattttgatt gttttcaga atctgcata 360
agaaaagcca tatttagaca cagagttagt cttaggttg aatatcgage aggacatagc 420
aaggtagat cactacagta ctggcaata gcagcattaa taacacccaa aaagataaag 480
ccacccttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggagcaca tacaatgaat ggacactag 579

<210> 30

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 30

atggaaaaca gatggcagggt gatgatttg tggcaggtag acaggatgag gattagaaca 60
tggacacgtt tagtaacata ccatatgtat agatcacaga aagctaggaa atggtttat 120
agacatcaat atcacatgtc tcatccaaaa gtaagtgtcag aagtcacat cccactagag 180
gtatcttagat tggcaataacc aacatffttg ggtctgcata caggagaaag agactggcat 240
ttgggtcagg gagtctccat agaaatgggg aaaaggagat atagcacaca agtagaccc 300
gtatctgcag accaactaat tcatctgtat tattttgatt gttttcaga atctgcata 360
agaaaagcca tatttagaca cagagttagt cttaggttg aatatcgage aggacatagc 420
aaggtagat cactacagta ctggcaata gcagcattaa taacacccaa aaagataaag 480
ccacccttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggagcaca tacaatgaat ggacactag 579

<210> 31

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 31

atggaaaaca gatggcagggt gatgatttg tggcaggtag acaggatgag gattagaaca 60
tggacacgtt tagtaaaata ccatatgtat agatcaaaa aagctaggaa atggtttat 120
agacatcaat atcaaaatgtc tcatccaaaa gtaagtgtcag aagtcacat cccactagag 180
gtatcttagat tggaaaataac aacatattgg ggtctgcata caggagaaag agactggcat 240
ttgggtcagg gagtctccat agaaatgggg aaaaggagat atagcacaca cgtgcaccc 300
gtatctgcag accaactaat tcatctgtat tattttgatt gtcttcaga atctgcata 360
agaaaagcca tatttagaca cagagttagt cttaggttg aatatcgage aggacatagc 420
aaggtagat cactacagta ctggcaata gcagcattaa taacacccaa aaagataaag 480
ccacccttgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gaggagcaca tacaatgaat ggacactag 579

<210> 32
<211> 579
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 32
atggaaaaca gatggcagggt gatgatttgt tgccaggtag acaggatgag gattagaaca 60
tggAACAGTT tagtaaaaata ccatATGtAT agatCAAAGA aAGCTAGGGAt ATGGTTTAt 120
agACATCAct atcaAAgTCC tCATCaaaaA gtaAGTCAG aAGTACACAT CCACTAGAG 180
gATGCTAGAT TGGTAATAAC AACATATTG GGTCTGCATA CAGGAGAAAG AGACTGGCAT 240
ttgggtcagg gagtctccat agaatggagg AAAAGGAGAT atagcacaca ctagacCCt 300
gatCTAGCAG ACCAATAcT tCATCTGtAT tATTTGATT GTTTcAGA ATCTGCTATA 360
agaaaAGCCa TATTAAGACA CAGAGTtAGT CTCAGGTGtG AATATCgAGC AGGACATAGC 420
aAGTAGGAT CACTACAGTA CTGGCAATA GCAGCATTAA TAACACCAAA AAAGATAAAG 480
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agACATCAct atcaAAgTCC tCATCaaaaA gtaAGTCAG aAGTACACAT CCACTAGAG 180
gATGCTAGAT TGGTAATAAC AACATATTG GGTCTGCATA CAGGAGAAAG AGACTGGCAT 240
ttgggtcagg gagtctccat agaatggagg AAAAGGAGAT atagcacaca agtagacCCt 300
gatCTAGCAG ACCAATAcT tCATCTGtAT tATTTGATT GTTTcAGA ATCTGCTATA 360
agaaaAGCCa TATTAAGACA CAGAGTtAGT CTCAGGTGtG AATATCgAGC AGGACATAGC 420
aAGTAGGAT CACTACAGTA CTGGCAATA GCAGCATTAA TAACACCAAA AAAGATAAAG 480
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<210> 34
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<223> Description of Artificial Sequence: Novel Sequence

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agacatcact atcaaaGTC tcatccaaaa gtaagtTCAG aagtacacat ccactagag 180
gtatGCTAGT tgtaataac aacattttg ggTCGCTATA caggagaAGG agactGGCAT 240
ttggTCAGG gagTCCTCAAG aagatGGAGG atagacacaca cgtGACACCT 300
gtatCAGCG accactaaAT tcATGTAT tattttGAT gtTTTCAGA atCTGCTATA 360
agaaaaGCA tattAGACA caGAGTAGT ctAGGTGt aataTCGAGC aggacatGAC 420
aaggatGGAT cactAGCA ctGGCAATA gcAGCATTAA taACACAAA aAGATAAAG 480
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aaggGTcaca gagggAGGCCA tacaaTGAAT ggacactAG 579

<210> 35

<211> 579

<212> DNA

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TTATAGACA TCACTATCAC AGCCCTCATC CAGAACAAAG TCAACAGCC CACATCCCGC 180
TAGGGATGG TAGATTGGAA AAAATAGCAG TTGGAGTCG GTGATACAGGA GATGGCGTCT 240
GGCACAGGGG GCACTGAGTC TCCATAGAAT GGAGGAAAAG GAGATATAGC ACACAAGTAG 300
ACCCTGATCT AGTAGACCAA CTAACTCATC TGTATTATT TGATGTTT TCAGAACCTG 360
CTATAAAGAA AGCATAATTAA GGACACAGAG TTAGTCCTAG GTGTGAATAA CGAGCAGGAC 420
ATAGCAAGGT AGGATCACTA CAGTACTTGG CAATAGCAGC ATTATAACA CCAAAAAAGA 480
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AGACATCACT ATGAAAGCCC TCACTCAAAAGA GTAGITCAA CAGCCACAT CCCGCTAGGG 180
GATGGTAGAT TGGAGAAAAC AGCACTTGG AGTCTGCAGG CAGGAGATGG AGTCTGGCAC 240
AGGGGGCCATC CAGTCCTCAT AGAAATGGAGG AAAAAGGAGAT ATAGCACACA AGTAGACCT 300
GATTGGTAG ACCAACTAATC TCACTGTAT TATTGTTGATT GTTTTCAGA ATCTGCTATA 360
AGAAAAGCCA TATTAGGATA TAGAGTGTGCT CTCAGGTGTG AATACCAAGC AGGACATAA 420
AAGGTAGAT CTCTACAGTA CTTGGCACTA GCACGTTAA TAACACCCAA GAAGATAAAG 480
CCACCTTGC CTAGTGTGAG GAAACTGACA GAGGATAGAT GGAACAAGCC CCAAGAGACC 540
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<210> 38

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<212> DNA

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GATGCTAGAT TGGTGATAAC AACATATTGG AGTCTGCATG CAGGAGAAATG AGACTGGCAT 240
GTGGGTCAAGA GAGTCCTCAT AGAAATGGAGG AAAAAGGAGAT ATAGCACACA AGTAGACCT 300
GACTTGGCAG ACCAACTAATC TCACTGTAT TATTGTTGATT GTTTTCAGA ATCTGCTATA 360

agaaaagcca tattaggata tagatgtgt cctagggtgt aataccaagc aggacataat 420
aaggtagat ctctacagta ctggcaacta gcagcattaa taacacccaa gaagataaag 480
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gtatgtat tggtaacac accatattgg ggttgc当地at gaggagaag agactggat 240
ctggc当地cagg gagtctccat agaatggagg aaaaggagat atagcacaca agtagaccc 300
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agaaaagcca tattaggata tagatgtgt cctagggtgt aataccaagc aggacataat 420
aaggtagat ctctacagta ctggcaacta gcagcattaa taacacccaa gaagataaag 480
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<210> 40

<211> 579

<212> DNA

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<223> Description of Artificial Sequence: Novel Sequence

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agaaaagcca tattaggata tagatgtgt cctagggtgt aataccaagc aggacataat 420
aaggtagat ctctacagta ctggcaacta gcagcattaa taacacccaa gaagataaag 480
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<211> 579

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gaccctggcag accaactaat tcattcgat tattttgatt gttttcaga atctgcata 360
agaaaagcca tatttagata tagatgtatg cttaggtgtg aatccaagc aggacataat 420
aaggtagat ctctacatg ctggcaacttgc gcaacttggaa gaggatagat ggaacaagcc 480
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gtatgtatg tggatataac aacatattgg ggtctgcattc caggagaag agactggcat 240
ttgggtcagg gagtctccat agaatggagg aaaaggat atagcacaca ctgtaccc 300
gaccctggcag accaactaat tcattcgat tattttgatt gttttcaga atctgcata 360
agaaaagcca tatttagata tagatgtatg cttaggtgtg aatccaagc aggacataat 420
aaggtagat ctctacatg ctggcaacttgc gcaacttggaa gaggatagat ggaacaagcc 480
ccacccatgc ctatgttgc gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
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<210> 43

<211> 579

<212> DNA

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aaggtagat ctctacatgtat cttggcacta gcacgtttaa taacacccaa gaagataaag 480
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<210> 44

<211> 578

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gtatctatgg tggagataac a acatattgg ggtctgcatt caggagaag agactggcat 240
ttgggtcagg gagtcctcat agaatggagg aaaaggat atagcacaca atgacacct 300
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aaggtagat ctctacatgtat cttggcacta gcacgtttaa taacacccaa gaagataaag 480
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<211> 579

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aaggtaggt ctctcagta ctggcacta geacgattaa taacacaaaa gaagataaag 480
ccacccatgc ctatgttgag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
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<210> 46

<211> 579

<212> DNA

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<223> Description of Artificial Sequence: Novel Sequence

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agacatacact atgaaagccc tcatccaaa gtaagttagc aagtacacat cccactagg 180
gtatcttagat tggatataa aacattttgg ggctcgatc caggagaag agactggcat 240
ttgggtcagg gagtcctcat aagatggagg aaaaggat atagcacaca agtagaccct 300
gacctggcagg accaactaat tcatcgat tattttgtt gttttcaga atctgcata 360
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aaggtaggt ctctcagta ctggcacta geacgattaa taacacaaaa gaagataaag 480
ccacccatgc ctatgttgag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggccaca gagggagcca tacaatgtt ggacactag 579

ATTENUATED VIF DNA IMMUNIZATION CASSETTES
FOR GENETIC VACCINES

ACKNOWLEDGMENT OF GOVERNMENT RIGHTS

This invention was made with Government support from the National
5 Institutes of Health. The Government has certain rights in this invention.

FIELD OF THE INVENTION

The invention relates to the preparation and use of attenuated, nonfunctional
HIV *vif* immunization cassettes as genetic vaccines for pathogenic genes.

BACKGROUND OF THE INVENTION

10 Vaccination and immunization generally refer to the introduction of a non-virulent agent against which an individual's immune system can initiate an immune response which will then be available to defend against challenge by a pathogen. The immune system identifies invading "foreign" compositions and agents primarily by identifying proteins and other large molecules which are not normally present in the individual. The foreign protein
15 represents a target against which the immune response is made.

The immune system can provide multiple means for eliminating targets that are identified as foreign. These means include humoral and cellular responses which participate in antigen recognition and elimination. Briefly, the humoral response involves B cells which produce antibodies that specifically bind to antigens. There are two arms of the
20 cellular immune response. The first involves helper T cells which produce cytokines and

elicit participation of additional immune cells in the immune response. The second involves killer T cells, also known as cytotoxic T lymphocytes (CTLs), which are cells capable of recognizing antigens and attacking the antigen including the cell or particle it is attached to.

Vaccination has been singularly responsible for conferring immune protection

- 5 against several human pathogens. In the search for safe and effective vaccines for immunizing individuals against infective pathogenic agents such as viruses, bacteria, and infective eukaryotic organisms, several strategies have been employed thus far. Each strategy aims to achieve the goal of protecting the individual against pathogen infection by administering to the individual, a target protein associated with the pathogen which can elicit
10 an immune response. Thus, when the individual is challenged by an infective pathogen, the individual's immune system can recognize the protein and mount an effective defense against infection. There are several vaccine strategies for presenting pathogen proteins which include presenting the protein as part of a non-infective or less infective agent or as a discreet protein composition.

- 15 One strategy for immunizing against infection uses killed or inactivated vaccines to present pathogen proteins to an individual's immune system. In such vaccines, the pathogen is either killed or otherwise inactivated using means such as, for example, heat or chemicals. The administration of killed or inactivated pathogen into an individual presents the pathogen to the individual's immune system in a noninfective form and the individual can
20 thereby mount an immune response against it. Killed or inactivated pathogen vaccines provide protection by directly generating T-helper and humoral immune responses against the pathogenic immunogens. Because the pathogen is killed or otherwise inactivated, there is little threat of infection.

- Another method of vaccinating against pathogens is to provide an attenuated
25 vaccine. Attenuated vaccines are essentially live vaccines which exhibit a reduced infectivity. Attenuated vaccines are often produced by passaging several generations of the pathogen through a permissive host until the progeny agents are no longer virulent. By using an attenuated vaccine, an agent that displays limited infectivity may be employed to elicit an immune response against the pathogen. By maintaining a certain level of infectivity, the
30 attenuated vaccine produces a low level infection and elicits a stronger immune response than killed or inactivated vaccines. For example, live attenuated vaccines, such as the poliovirus

and smallpox vaccines, stimulate protective T-helper, T-cytotoxic, and humoral immunities during their nonpathogenic infection of the host.

Another means of immunizing against pathogens is provided by recombinant vaccines. There are two types of recombinant vaccines: one is a pathogen in which specific genes are deleted in order to render the resulting agent non-virulent. Essentially, this type of recombinant vaccine is attenuated by design and requires the administration of an active, non-virulent infective agent which, upon establishing itself in a host, produces or causes to be produced antigens used to elicit the immune response. The second type of recombinant vaccine employs infective non-virulent vectors into which genetic material that encode target antigens is inserted. This type of recombinant vaccine similarly requires the administration of an active infective non-virulent agent which, upon establishing itself in a host, produces or causes to be produced, the antigen used to elicit the immune response. Such vaccines essentially employ infective non-virulent agents to present pathogen antigens that can then serve as targets for an anti-pathogen immune response. For example, the development of vaccinia as an expression system for vaccination has theoretically simplified the safety and development of infectious vaccination strategies with broader T-cell immune responses.

Another method of immunizing against infection uses subunit vaccines. Subunit vaccines generally consist of one or more isolated proteins derived from the pathogen. These proteins act as target antigens against which an immune response may be mounted by an individual. The proteins selected for subunit vaccine are displayed by the pathogen so that upon infection of an individual by the pathogen, the individuals immune system recognizes the pathogen and mounts a defense against it. Because subunit vaccines are not whole infective agents, they are incapable of becoming infective. Thus, they present no risk of undesirable virulent infectivity that is associated with other types of vaccines. It has been reported that recombinant subunit vaccines such as the hepatitis B surface antigen vaccine (HBsAg) stimulate a more specific protective T-helper and humoral immune response against a single antigen. However, the use of this technology to stimulate board protection against diverse pathogens remains to be confirmed.

The construction of effective vaccines is complicated by several factors which include the pathobiology of the pathogen and the specificities of the of the host immune response. Recently a novel tool for understanding the immune component in these

interactions has become available in the form of genetic immunization or DNA vaccination.

Tang, *et al.*, *Nature*, **1992**, *356*, 152; Fynan, *et al.*, *Proc. Natl. Acad. Sci. USA*, **1993**, *90*,

11478; Ulmer, *et al.*, *Science*, **1993**, *259*, 1745; and Wang, *et al.*, *Proc. Natl. Acad. Sci. USA*,

1993, *90*, 4156. The ability of this approach was demonstrated to produce broad immune

5 responses against structural and enzymatic gene products of HIV-1 and outlined a strategy

for development of a possible prophylactic vaccine for HIV-1. This strategy utilized multiple

gene expression cassettes encoding *gag/pol/rev* as well as *env/rev* and accessory gene

immunogens. Studies clearly demonstrated that rodents and primates can be successfully

immunized with HIV-1 structural and envelope genes. Wang, *et al.*, *Proc. Natl. Acad. Sci.*

10 *USA*, **1993**, *90*, 4156 and Wang, *et al.*, *DNA Cell Biol.*, **1993**, *12*, 799. A genetic strategy for

construction of immunogen expression cassettes from a pathogenic gene which can be broadly applied in order to use DNA immunogens against a variety of pathogens is needed.

Primate lentiviral genomes contain genes encoding novel regulatory and accessory proteins as well as proteins with structural and enzymatic functions. The regulatory

15 genes, *tat* and *rev*, and the accessory genes, *nef*, *vif*, *vpr*, *vpu*, and *vpx*, are well conserved in

many lentiviruses, including HIV and SIV. The well conserved nature of these genes implies

that their protein products play a critical role in viral pathogenesis *in vivo*. Initial *in vitro*

experiments seemed to demonstrate that *tat* and *rev* were essential for viral replication, while

the accessory genes were considered nonessential. Cullen, *et al.*, *Cell*, **1989**, *58*, 423 and

20 Desrosiers, *AIDS Res. Human Retroviruses*, **1992**, *8*, 411. Further analyses, however, has

revealed that defects within the accessory gene result in severe impairment or delay in viral

replication *in vitro* (Gabudza, *et al.*, *J. Virol.*, **1992**, *66*, 6489 and Gibbs, *et al.*, *AIDS Res.*

Human Retroviruses, **1994**, *10*, 343) and *in vivo* (Aldrovandi, *et al.*, *J. Virol.*, **1996**, *70*,

1505). Native defective accessory genes have been reported *in vivo* and may be an end

25 product of an effective host immune response. The accessory genes are, therefore, presently

considered to be determinants of virus virulence. Trono, *Cell*, **1995**, *82*, 189. They contain

few "hotspots" and may be less susceptible to mutations leading to the production of "escape"

virus variants, emphasizing their importance in the viral life cycle. In addition, the protein

products of these genes are immunogenic *in vivo*. As a group, they represent twenty percent

30 of the possible anti-viral immune targets. Ameisen, *et al.*, *Int. Conf. AIDS*, **1989**, *5*, 533 and

Lamhamdi-Cherradi, *et al.*, *AIDS*, **1992**, *6*, 1249. Their immunogenicity and low functional

mutagenicity combine to make the accessory genes attractive elements in the design of future anti-viral immune therapeutics. The production of accessory gene immunogens poses specific immunologic and pathogenic complications for a viral vaccine design, however, due to the role of the accessory gene protein products as determinants of viral virulence. A potential 5 accessory gene-based genetic vaccine would need to be accessible to the host's immune response against native viral accessory gene products without enhancing viral replication. Accordingly, a major goal is to design a safe and effective genetic anti-HIV vaccine, which includes the *vif* (virion infectivity factor) accessory gene as part of a multi-component genetic immunogen.

10 The *vif* gene encodes a 23 kDa late viral protein (*vif*) from a singly spliced, rev-dependent 5 kb transcript. Arya, *et al.*, *Proc. Natl. Acad. Sci. USA*, **1986**, *83*, 2209; Garrett, *et al.*, *J. Virol.*, **1991**, *65*, 1653; Schwartz, *et al.*, *Virology*, **1991**, *183*, 677; and Sodroski, *et al.*, *Science*, **1986**, *231*, 1549. *Vif* is highly conserved among HIV-1 isolates and is present in other lentiviruses, such as Feline Immunodeficiency Virus (FIV), Bovine 15 Immunodeficiency Virus (BIV), Visna virus, HIV-2, and SIV. Myers, *et al.*, *Human Retrovir. AIDS*, **1991** and Shackett, *et al.*, *Virology*, **1994**, *204*, 860. Earlier analyses of *in vivo* *vif* genetic variation have shown that most *vif* sequences are intact reading frames and the presence of intact *vif* does not have a correlation with disease status. Sova, *et al.*, *J. Virol.*, **1995**, *69*, 2557 and Wieland, *et al.*, *Virology*, **1994**, *203*, 43. However, sequential analyses of 20 a region containing *vif*, *vpr*, *vpu*, *tat*, and *rev* genes from a HIV-1 infected long-term progressor revealed the presence of inactivating mutations in 64% of the clones. Michael, *et al.*, *J. Virol.*, **1995**, *69*, 4228. HIV-1 infected subjects have been shown to carry antibodies which recognize recombinant *vif* protein (Kan, *et al.*, *Science*, **1986**, *231*, 1553; Schwander, *et al.*, *J. Med. Virol.*, **1992**, *36*, 142; and Wieland, *et al.*, *AIDS Res. Human Retrovir.*, **1991**, *7*, 861) suggesting that the protein is expressed and is immunogenic during natural infection (Volsky, *et al.*, *Curr. Topics Micro. Immunol.*, **1995**, *193*, 157).

30 Due to *vif*'s ability to activate viral replication in *trans*, an attenuated genetic vaccine design, similar to those utilized in the production of vaccines derived from toxic viral, bacterial, or parasitic components was employed in the present invention. The sequence variation and immunogenic potential present in *vif* genes derived from HIV-1 infected subjects was analyzed. Prototypic genetic variants were selected and the ability of those

clones to induce humoral and cellular immune responses was studied in animals. The selected *vif* genetic variants were also functionally characterized through transcomplementation assays utilizing cells infected with a vif-defective HIV-1 clone. Attenuated, nonfunctional *vif* clones are demonstrated to induce immune responses capable of destroying native pathogen.

5 SUMMARY OF THE INVENTION

The present invention relates to a purified attenuated, non-functional *vif* protein.

The present invention relates to a *vif* protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,

- 10 SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, and SEQ ID NO:23.

The present invention relates to an isolated nucleic acid molecule comprising
15 a nucleotide sequence encoding an attenuated, non-functional *vif* protein.

The present invention relates to a nucleic acid molecule encoding a *vif* protein which comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.

The present invention relates to a nucleic acid molecule encoding a *vif* protein which comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID

- 25 NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

The present invention relates to a pharmaceutical composition comprising the nucleic acid molecule encoding an attenuated, non-functional *vif* protein in a pharmaceutically acceptable carrier or diluent.

- 30

The present invention relates to a recombinant expression vector comprising a nucleic acid molecule comprising a nucleotide sequence encoding an attenuated, non-functional *vif* protein.

The present invention relates to a host cell comprising a recombinant expression vector comprising a nucleic acid molecule encoding an attenuated, non-functional *vif* protein

The present invention relates to a purified antibody directed against an attenuated, non-functional *vif* protein.

The present invention relates to a method of immunizing a mammal against a virus comprising administering to cells of said mammal, a nucleic acid molecule that comprises a nucleotide sequence that encodes an attenuated, non-functional *vif* protein, wherein said nucleic acid molecule is expressed in said cells.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows a comparison of the deduced amino acid sequences of *vif* derived from transmitter and non-transmitter mothers with well characterized HIV-1 molecular clones PNL43, SF-2, and Zr6. T-#, clones from transmitter subject; N-#, clones from non-transmitter subject; --, identity with the consensus sequence (Con; SEQ ID NO:1); .., represents gap; *, a stop codon.

Figure 2 shows a 10% SDS-PAGE of immunoprecipitates. Expression of HIV-1 *vif* clones derived from transmitter and non-transmitter mothers. *Vif* expression plasmids were used for coupled *in vitro* transcription/translation according to the manufacturer's instructions (Promega). Immunoprecipitation of the *in vitro* translated proteins was performed with *vif* antiserum as described herein. The designation of the *vif* clones is indicated on the top. The clone numbers designated with T-** and N-** are derived from the transmitter and non-transmitter mothers respectively. pCVif is the *vif* expression plasmid of HIV-1_{SF2}.

Figures 3A and 3B show the results of an enzyme linked immunoabsorbent assay (ELISA) of anti-*vif* antibody responses in mice after immunization with a DNA construct expressing *vif*. Mouse sera was diluted in blocking buffer at a dilution of 1:500 and

assayed as described herein. In Figure 3A, mice were immunized with 50 µg of DNA. In Figure 3B, mice were immunized with 100 µg of DNA per injection.

Figure 4 shows the results of a chromium release assay whereby lysis of murine targets (p815) expressing *vif* protein by splenocytes from mice immunized with *vif* expression constructs. p815 cells (1×10^5 /ml) were infected with vaccinia expressing *vif* (VV:gag) and incubated for 16 hours to express the Vif protein. The target cells were labeled with ^{51}Cr for 1-2 hours and used to incubate the stimulated splenocytes for 6 hours. Specific lysis (%) was calculated according to the formula described herein.

Figures 5A, 5B, 5C and 5D show the results of a chromium release assay whereby lysis of HeLa CD4+/D^d cells infected with clinical HIV-1 isolate by splenocytes from mice immunized with *vif* expression cassette. HeLa CD4+/D^d cells (10^6) were infected with cell-free HIV-1 clinical isolate followed by a week incubation to allow the cells to infect and express viral proteins. One week postinfection, the target cells were labeled with ^{51}Cr for 1-2 hours and used to incubate the stimulated splenocytes for 6 hours. Specific lysis (%) was calculated according to the formula described herein.

Figure 6 shows the results of a proliferation assay showing activation and T cell proliferative response to recombinant Vif. Recombinant Vif (10 µg/ml) was plated in each well to stimulate proliferation of T cells. Lectin PHA (10 µg/ml) was used as a polyclonal stimulator positive control. Stimulation index was calculated as the level of radioactivity detected from the cells stimulated with specific protein divided by the level detected from the cells in media. Lanes 1a and 1b are from mice immunized with 50 and 100 µg of pCVif; Lanes 2a and 2b are from mice immunized with 50 and 100 µg of clone T-35; Lanes 2a and 2b are from mice immunized with 50 and 100 µg of clone N-15.

Figures 7A-7F show the amino acid sequences of preferred attenuated, non-functional *vif* proteins of the present invention.

Figures 8A-8E show the nucleotide sequences of preferred attenuated, non-functional *vif* proteins of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

One of the major goals of AIDS research is the development of a vaccine against the HIV-1 virus. An effective vaccine should elicit strong humoral response along

with an efficient and broad CTL response. This task is complicated because of the genetic heterogeneity of the HIV-1 virus. HIV-1 reverse transcriptase (RT) is prone to error and lacks the ability to proof-read, resulting in a mutation rate of 10^{-4} per cycle per genome.

Dougherty, *et al.*, *J. Virol.*, **62**, 2817. HIV-1 genome sequence variation has been observed

- 5 in viruses isolated from different individuals as well as in virus isolated from a single person at different time points. Fisher, *et al.*, *Nature*, **1988**, *334*, 444 and Meyerhans, *et al.*, *Cell*, **1989**, *58*, 901. Based upon a large number of sequence analysis data, it is apparent that the structural genes *env*, *gag* and *pol* are the major target for mutations which lead to escape-variant viruses in patients by changing the neutralizing antibody and/or CTL epitopes.
- 10 Pircher, *et al.*, *Nature*, **1990**, *346*, 629; Reitz, *et al.*, *Cell*, **1988**, *54*, 57; and Wolfs, *et al.*, *Virol.*, **1991**, *185*, 195. Despite this, earlier experiments have indicated that structural and enzymatic genes of HIV-1 can be used successfully as nucleic acid-based vaccines in different animal models (Wang, *et al.*, *Proc. Natl. Acad. Sci. USA*, **1993**, *90*, 4156; and Wang, *et al.*, *AIDS*, **1995**, *9* (*Suppl A*), S159) and prophylactic as well as therapeutic studies for DNA
- 15 vaccines have commenced. The present invention is directed to development of *vif*, a HIV-1 accessory gene, as an immunogen cassette. When used in concert with other HIV-1 genes a broad immune response against all viral components may be induced, thus mimicking many aspects of the immune responses induced by a live attenuated vaccine.

In the present invention, induction of *vif*-specific humoral and cellular immune

- 20 responses in mice have been observed to directly correlate with the concentration of DNA injected and number of boosts. Similar results were observed in T-cell proliferation and CTL assays, demonstrating that *vif* genes are immunogenic *in vivo*. *Vif* is known to present in both soluble and membrane associated form. Goncalves, *et al.*, *J. Virol.*, **1994**, *68*, 704. Although anti-*vif* antibodies and *vif*-specific CTL responses have been shown in HIV-1 positive
- 25 patients, epitopes involved in the presentation of *vif* to the immune system have not yet been defined. Lamhamedi-Cherradi, *et al.*, *AIDS*, **1992**, *6*, 1249. How *vif* becomes exposed to the humoral immune system is unclear in these studies. The observed different immune response in the clones of the present invention suggest that the mutations in T-35, N-15 and pCVif may be associated with changes in antibody/CTL responses.

- 30 It is significant to note that some the point mutations present in all the T or N derived clones indicate that these mutations may be responsible for the difference in

complementation and/or immune responses observed. Further mutational analysis of vif help resolve answer the regions involved in complementation. Proposed sites of vif activity include viral DNA synthesis, gpl20 synthesis and transport, and gag processing. Borman, *et al.*, *J. Virol.*, **1995**, 69, 2058; Sakai, *et al.*, *J. Virol.*, **1993**, 67, 1663; and Von Schwedler, *et al.*, *J. Virol.*, **1993**, 67, 4945. Transcomplementation experiments with vif-defective HIV-1 provirus and wild-type HIV-1 vif-expressing cell lines indicate that vif acts at a late stage in virus replication/maturation and that vif transcomplementation occurs across HIV-1 strains. Blanc, *et al.*, *Virol.*, **1993**, 193, 186 and Hevey, *et al.*, *Virus Res.*, **1994**, 33, 269. Earlier experiments have shown that sera from the nontransmitter subject (N1) contains a high antibody titer against envelope protein and nonreplicating virus; whereas sera from the transmitter patient (T1) contains very low antibody titers against envelop proteins and highly replicating virus. Velpandi, *et al.*, *DNA Cell Biol.*, **1996**, 15, 571. These results correlate with the trans-complementation results observed in the present invention.

The present invention relates to isolated nucleic acid molecules comprising a nucleotide sequence encoding an attenuated, non-functional vif protein. As used herein, the term "attenuated, non-functional vif protein" is meant to refer to vif proteins that have no or reduced virion infectivity function compared to wild-type vif. In some embodiments of the invention, the nucleic acid molecules encode an attenuated, non-functional vif protein wherein the nucleotide sequence comprises deletions, additions, a point mutation(s), multiple substitutions, or introduction of a stop codon to render a shortened protein. In preferred embodiments of the invention, the isolated nucleic acid molecules of the invention encode a vif protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23. In other preferred embodiments of the invention, the isolated nucleic acid molecules encode a vif protein and comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID

NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

The nucleic acid molecules of the invention may be obtained from patients infected with the human immunodeficiency virus as described below in the Examples.

- 5 Alternatively, the nucleic acid molecules of the invention may be prepared using the wild-type *vif* nucleotide sequence. The *vif* expression plasmid, pCVif, contains the *vif* gene from the well-characterized HIV-1 molecular clone, pHXB2, under the control of the cytomegalovirus (CMV) immediate early promoter, within the backbone plasmid, pRc/CMV (Invitrogen, San Diego, CA) as described in Nagashunmugam, *et al.*, *DNA Cell Biol.*, **1996**,
- 10 15,353, incorporated herein by reference. This nucleic acid molecule may be used to prepare additional nucleic acid molecules encoding attenuated, non-functional *vif* proteins.

A number of methods can be used to design specific mutations in wild-type nucleic acid molecules to produce nucleic acid molecules encoding attenuated, non-functional *vif* proteins. For example, oligonucleotide-mediated mutagenesis is commonly used to add, 15 delete, or substitute nucleotides in a segment of DNA whose sequence is known. Such methods are taught in, for example, Sambrook *et al.*, *Molecular Cloning a Laboratory Manual*, Second Ed. Cold Spring Harbor Press (1989), pages 15.51 to 15.73, which is incorporated herein by reference. Briefly, the protocol for oligonucleotide-mediated mutagenesis involves the following steps: 1) cloning of an appropriate fragment of DNA, 20 such as the *vif* nucleotide sequence from the pCVif expression plasmid, into a bacteriophage M13 vector; 2) preparation of single-stranded DNA from the recombinant bacteriophage M13; 3) design and synthesis of mutagenic oligonucleotides; 4) hybridization of the mutagenic oligonucleotides to the target DNA; 5) extension of the hybridized oligonucleotide by DNA polymerase; 6) transfection of susceptible bacteria; 7) screening of bacteriophage 25 plaques for those carrying the desired mutation; 8) preparation of single-stranded DNA from the mutagenized recombinant bacteriophage; 9) confirmation by sequencing that the mutagenized bacteriophage M13 DNA carries the desired mutation and no other mutation; 10) recovery of the mutated fragment of DNA from the double-stranded replicative form of the recombinant bacteriophage M13; and 11) substitution of the mutagenized fragment for 30 the corresponding segment of wild-type DNA in the desired expression vector.

Design and synthesis of the mutagenic oligonucleotides, which are tailored to the desired mutation in the nucleic acid molecule encoding *vif*, is described in detail in, for example, Sambrook et al., *Molecular Cloning a Laboratory Manual*, Second Ed. Cold Spring Harbor Press (1989), pages 15.54 to 15.56, which is incorporated herein by reference. For example, to substitute, add, or delete a single nucleotide into the wild-type *vif* nucleotide sequence, oligonucleotides of about 17-19 nucleotides in length which carry the mismatched nucleotide at the center or at one of the two nucleotide positions immediately 3' of the center are prepared. To substitute, add, or delete two or more contiguous nucleotides into the wild-type *vif* nucleotide sequence, oligonucleotides of about 25 or more nucleotides in length are prepared. These oligonucleotides comprise about 12 to 15 perfectly matched nucleotides on either side of the central looped-out region which contains the added or substituted nucleotides, or represents the portion of the wild-type DNA that is looped out. Using the strategy described above, one skilled in the art can prepare nucleic acid molecules having deletions, additions, substitutions, or premature stop codons, which encode attenuated, non-functional *vif* proteins. Oligonucleotide-mediated mutagenesis procedures are widely known to those skilled in the art.

Alternately, the nucleic acid molecules of the invention can be prepared using DNA synthesizers by standard DNA methodology. One skilled in the art readily understands that the genetic code is degenerate and, therefore, could prepare numerous DNA sequences encoding the same protein. In addition, one skilled in the art readily understands that amino acids can be substituted by other amino acids such that conservative substitutions are made. Accordingly, one skilled in the art can prepare nucleic acid molecules of the invention encoding attenuated, non-functional *vif* proteins.

Preferred nucleic acid molecules of the invention encode attenuated, non-functional *vif* proteins having the amino acid (a.a.) and nucleotide sequences (nt.) (represented by particular SEQ ID Numbers) in Table 1. The specific amino acid sequences are shown in Figure 1 and Figures 7A-7F. The specific nucleotide sequences are shown in Figures 8A-8E.

Table 1

Vif Protein	SEQ ID NO:		Vif Protein	SEQ ID NO:		
	a.a.	nt.		a.a.	nt.	
N13	4	27	T3	14	37	
N15	5	28	T4	15	38	
5	N17	6	29	T35	16	39
	N22	7	30	T37	17	40
	N23	8	31	T38	18	41
	N24	9	32	T39	19	42
	N26	10	33	T40	20	43
	N27	11	34	T42	21	44
	N29	12	35	T43	22	45
	N30	13	36	T44	23	46

- The present invention also relates to vectors or recombinant expression vectors that comprise a nucleotide sequence that encodes an attenuated, non-functional *vif* protein.
- 15 As used herein, the term "recombinant expression vector" is meant to refer to a plasmid, phage, viral particle or other vector which, when introduced into an appropriate host, contains the necessary genetic elements to direct expression of the coding sequence that encodes an attenuated, non-functional *vif* protein. In some embodiments of the invention, the vector or recombinant expression vector encodes an attenuated, non-functional *vif* protein wherein the
- 20 nucleotide sequence comprises deletions, additions, point mutation(s), multiple substitutions, or introduction of a stop codon to render a shortened protein. In preferred embodiments of the invention, the vectors or recombinant expression vectors of the invention encode a *vif* protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23. In other preferred embodiments of the invention, the vectors or recombinant expression vectors of the invention comprise a nucleic

- acid molecule encoding a *vif* protein which comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, 5 SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

One having ordinary skill in the art can isolate the nucleic acid molecule that encodes an attenuated, non-functional *vif* protein and insert it into an expression vector using standard techniques and readily available starting materials. The coding sequence is operably linked to the necessary regulatory sequences. Expression vectors are well known and readily 10 available. Examples of expression vectors include plasmids, phages, viral vectors and other nucleic acid molecules or nucleic acid molecule containing vehicles useful to transform host cells and facilitate expression of coding sequences. The recombinant expression vectors of the invention are useful for transforming hosts which express an attenuated, non-functional *vif* protein.

- 15 The present invention also relates to a host cell that comprises the recombinant expression vector that includes a nucleotide sequence that encodes an attenuated, non-functional *vif* protein. In some embodiments of the invention, the host cell comprises the vector or recombinant expression vector that encodes an attenuated, non-functional *vif* protein wherein the nucleotide sequence comprises deletions, additions, point mutation(s), multiple 20 substitutions, or introduction of a stop codon to render a shortened protein. In preferred embodiments of the invention, the host cells comprises vectors or recombinant expression vectors that encode a *vif* protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID 25 NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23. In other preferred embodiments of the invention, the host cell comprises vectors that comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, 30 SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45

and SEQ ID NO:46. Host cells for use in well known recombinant expression systems for production of proteins are well known and readily available.

- The most commonly used prokaryotic system remains *E. coli*, although other systems such as *B. subtilis* and *Pseudomonas* are also useful. Suitable control sequences for 5 prokaryotic systems include both constitutive and inducible promoters including the *lac* promoter, the *trp* promoter, hybrid promoters such as tac promoter, the *lambda* phage P1 promoter. In general, foreign proteins may be produced in these hosts either as fusion or mature proteins. When the desired sequences are produced as mature proteins, the sequence produced may be preceded by a methionine which is not necessarily efficiently removed.
- 10 Accordingly, the peptides and proteins claimed herein may be preceded by an N-terminal Met when produced in bacteria. Moreover, constructs may be made wherein the coding sequence for the peptide is preceded by an operable signal peptide which results in the secretion of the protein. When produced in prokaryotic hosts in this manner, the signal sequence is removed upon secretion. Examples of prokaryotic host cells include bacteria cells such as *E. coli*, and 15 yeast cells such as *S. cerevisiae*.
- A wide variety of eukaryotic hosts are also now available for production of recombinant foreign proteins. As in bacteria, eukaryotic hosts may be transformed with expression systems which produce the desired protein directly, but more commonly signal sequences are provided to effect the secretion of the protein. Eukaryotic systems have the 20 additional advantage that they are able to process introns which may occur in the genomic sequences encoding proteins of higher organisms. Eukaryotic systems also provide a variety of processing mechanisms which result in, for example, glycosylation, carboxy-terminal amidation, oxidation or derivatization of certain amino acid residues, conformational control, and so forth. Commonly used eukaryotic systems include, but are not limited to, yeast, fungal 25 cells, insect cells, mammalian cells, avian cells, and cells of higher plants. In preferred embodiments of the invention insect cells such as *S. frugiperda*, non-human mammalian tissue culture cells chinese hamster ovary (CHO) cells and human tissue culture cells such as HeLa cells are used as host cells. Suitable promoters are available which are compatible and operable for use in each of these host types as well as are termination sequences and 30 enhancers, as e.g. the baculovirus polyhedron promoter. As above, promoters can be either

constitutive or inducible. For example, in mammalian systems, the mouse metallothionein promoter can be induced by the addition of heavy metal ions.

In some embodiments, for example, one having ordinary skill in the art can, using well known techniques, insert DNA molecules into a commercially available expression

- 5 vector for use in well known expression systems. For example, the commercially available plasmid pSE420 (Invitrogen, San Diego, CA) may be used for production of an attenuated, non-functional *vif* protein in *E. coli*. The commercially available plasmid pYES2 (Invitrogen, San Diego, CA) may, for example, be used for production in *S. cerevisiae* strains of yeast. The commercially available MAXBACT™ complete baculovirus expression system
- 10 (Invitrogen, San Diego, CA) may, for example, be used for production in insect cells. The commercially available plasmid pcDNA 1 or pcDNA3 (Invitrogen, San Diego, CA) may, for example, be used for production in mammalian cells such as Chinese Hamster Ovary cells. One having ordinary skill in the art can use these commercial expression vectors and systems or others to produce an attenuated, non-functional *vif* protein by routine techniques and
- 15 readily available starting materials. See e.g., Sambrook et al., *Molecular Cloning a Laboratory Manual*, Second Ed. Cold Spring Harbor Press (1989), which is incorporated herein by reference.

- One having ordinary skill in the art may use other commercially available expression vectors and systems or produce vectors using well known methods and readily
- 20 available starting materials. Expression systems containing the requisite control sequences, such as promoters and polyadenylation signals, and preferably enhancers, are readily available and known in the art for a variety of hosts. See e.g., Sambrook et al., *Molecular Cloning a Laboratory Manual*, Second Ed. Cold Spring Harbor Press (1989).

- Examples of genetic constructs include the attenuated, non-functional *vif*
- 25 protein coding sequence operably linked to a promoter that is functional in the cell line into which the constructs are transfected. Examples of constitutive promoters include promoters from cytomegalovirus or SV40. Examples of inducible promoters include mouse mammary leukemia virus or metallothionein promoters. Those having ordinary skill in the art can readily produce genetic constructs useful for transfecting with cells with DNA that encodes
 - 30 an attenuated, non-functional *vif* protein from readily available starting materials. Such gene constructs are useful for the production of an attenuated, non-functional *vif* protein.

Nucleic acid molecules that encode an attenuated, non-functional *vif* protein may be delivered to cells using any one of a variety of delivery components, such as recombinant viral expression vectors or other suitable delivery means, so as to affect their introduction and expression in compatible host cells. In general, viral vectors may be DNA 5 viruses such as recombinant adenoviruses and recombinant vaccinia viruses or RNA viruses such as recombinant retroviruses. Other recombinant vectors include recombinant prokaryotes which can infect cells and express recombinant genes. In addition to recombinant vectors, other delivery components are also contemplated such as encapsulation in liposomes, transferrin-mediated transfection and other receptor-mediated means. The invention is 10 intended to include such other forms of expression vectors and other suitable delivery means which serve equivalent functions and which become known in the art subsequently hereto.

In a preferred embodiment of the present invention, DNA is delivered to competent host cells by means of an adenovirus. One skilled in the art would readily understand this technique of delivering DNA to a host cell by such means. Although the 15 invention preferably includes adenovirus, the invention is intended to include any virus which serves equivalent functions.

In another preferred embodiment of the present invention, RNA is delivered to competent host cells by means of a retrovirus. One skilled in the art would readily understand this technique of delivering RNA to a host cell by such means. Any retrovirus 20 which serves to express the protein encoded by the RNA is intended to be included in the present invention.

In another preferred embodiment of the present invention, nucleic acid is delivered through folate receptor means. The nucleic acid sequence to be delivered to a host cell is linked to polylysine and the complex is delivered to the tumor cell by means of the 25 folate receptor. U.S. Patent 5,108,921 issued April 28, 1992 to Low *et al.*, which is incorporated herein by reference, describes such delivery components.

The present invention is also related to purified attenuated, non-functional *vif* proteins. The *vif* proteins of the invention have deletions, additions, point mutation(s), multiple substitutions, or introduction of stop codons to produce peptides that are attenuated 30 and non-functional compared to wild type *vif* protein. In preferred embodiments of the invention, the attenuated, non-functional *vif* proteins of the invention comprise an amino acid

- sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ
5 ID NO:23. In other preferred embodiments of the invention, the attenuated, non-functional *vif* proteins of the invention consist of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
10 SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23. The *vif* proteins of the invention may be prepared by routine means using readily available starting materials as described above.

The particulars for the construction of expression systems suitable for desired hosts are known to those in the art and are described above. For recombinant production of
15 the protein, the DNA encoding it is suitably ligated into the expression vector of choice and then used to transform the compatible host which is then cultured and maintained under conditions wherein expression of the foreign gene takes place. The proteins of the present invention thus produced are recovered from the culture, either by lysing the cells or from the culture medium as appropriate and known to those in the art. One having ordinary skill in
20 the art can, using well known techniques, isolate an attenuated, non-functional *vif* protein that is produced using such expression systems. Methods of purifying an attenuated, non-functional *vif* protein from natural sources using antibodies which specifically bind to an attenuated, non-functional *vif* protein may be equally applied to purifying an attenuated, non-functional *vif* protein produced by recombinant DNA methodology.

25 In addition to producing these proteins by recombinant techniques, automated amino acid synthesizers may also be employed to produce *vpr* protein. It should be further noted that if the proteins herein are made synthetically, substitution by amino acids which are not encoded by the gene may also be made. Alternative residues include, for example, the ω amino acids of the formula $H_2N(CH_2)_nCOOH$ wherein n is 2-6. These are neutral, nonpolar
30 amino acids, as are sarcosine (Sar), t-butylalanine (t-BuAla), t-butylglycine (t-BuGly), N-methyl isoleucine (N-MeIle), and norleucine (Nleu). Phenylglycine, for example, can be

substituted for Trp, Tyr or Phe, an aromatic neutral amino acid; citrulline (Cit) and methionine sulfoxide (MSO) are polar but neutral, cyclohexyl alanine (Cha) is neutral and nonpolar, cysteic acid (Cya) is acidic, and ornithine (Orn) is basic. The conformation conferring properties of the proline residues may be obtained if one or more of these is
5 substituted by hydroxyproline (Hyp).

Pharmaceutical compositions according to the invention comprise a pharmaceutically acceptable carrier in combination with either an attenuated, non-functional *vif* protein or a nucleic acid molecule of the invention encoding the same. In preferred embodiments of the invention, the pharmaceutical composition comprises a recombinant
10 expression vector that encodes a *vif* protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.

15 In other preferred embodiments of the invention, the pharmaceutical composition comprises a nucleic acid molecule encoding a *vif* protein which comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39,
20 SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46. Pharmaceutical formulations are well known and pharmaceutical compositions comprising the compounds of the invention may be routinely formulated by one having ordinary skill in the art. Suitable pharmaceutical carriers are described in *Remington's Pharmaceutical Sciences*, A. Osol, a standard reference text in this field, which is
25 incorporated herein by reference in its entirety.

The present invention also relates to an injectable pharmaceutical composition that comprises a pharmaceutically acceptable carrier and a compound of the present invention. The compound of the invention is preferably sterile and combined with a sterile pharmaceutical carrier. In some embodiments, for example, the compounds of the invention
30 can be formulated as a solution, suspension, emulsion or lyophilized powder in association with a pharmaceutically acceptable vehicle. Examples of such vehicles are water, saline,

Ringer's solution, dextrose solution, and 5% human serum albumin. Liposomes and nonaqueous vehicles such as fixed oils may also be used. The vehicle or lyophilized powder may contain additives that maintain isotonicity (e.g., sodium chloride, mannitol) and chemical stability (e.g., buffers and preservatives). The formulation is sterilized by commonly used
5 techniques.

An injectable composition may comprise a compound of the invention in a diluting agent such as, for example, sterile water, electrolytes/dextrose, fatty oils of vegetable origin, fatty esters, or polyols, such as propylene glycol and polyethylene glycol. The injectable must be sterile and free of pyrogens.

- 10 Formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Compositions for oral administration include powders or granules, suspensions or solutions in water or non-aqueous media, capsules, sachets or tablets.
15 Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids or binders may be desirable. Compositions for parenteral, intrathecal or intraventricular administration may include sterile aqueous solutions which may also contain buffers, diluents and other suitable additives.

The pharmaceutical compositions of the present invention may be administered
20 by any means that enables the active agent to reach the agent's site of action in the body of a mammal. The pharmaceutical compositions of the present invention may be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic, vaginal, rectal, intransal, transdermal), oral or parenteral. Parenteral administration includes intravenous
25 drip, subcutaneous, intraperitoneal or intramuscular injection, pulmonary administration, e.g., by inhalation or insufflation, or intrathecal or intraventricular administration.

Dosage varies depending upon known factors such as the pharmacodynamic characteristics of the particular agent, and its mode and route of administration; age, health, and weight of the recipient; nature and extent of symptoms, kind of concurrent treatment,
30 frequency of treatment, and the effect desired. Formulation of therapeutic compositions and their subsequent administration is believed to be within the skill of those in the art.

According to the invention, the pharmaceutical composition comprising a nucleic acid molecule that encodes a *vif* protein of the invention may be administered directly into the individual or delivered *ex vivo* into removed cells of the individual which are reimplanted after administration. By either route, the genetic material is introduced into cells which are present in the body of the individual. Preferred routes of administration include intramuscular, intraperitoneal, intradermal and subcutaneous injection. Alternatively, the pharmaceutical composition may be introduced by various means into cells that are removed from the individual. Such means include, for example, transfection, electroporation and microparticle bombardment. After the nucleic acid molecule is taken up by the cells, they are reimplanted into the individual.

The pharmaceutical compositions according to this aspect of the present invention comprise about 0.1 to about 1000 micrograms of DNA. In some preferred embodiments, the pharmaceutical compositions contain about 1 to about 500 micrograms of DNA. In some preferred embodiments, the pharmaceutical compositions contain about 25 to about 250 micrograms of DNA. Most preferably, the pharmaceutical compositions contain about 100 micrograms DNA.

The pharmaceutical compositions according to this aspect of the present invention are formulated according to the mode of administration to be used. One having ordinary skill in the art can readily formulate a nucleic acid molecule that encodes a *vif* protein of the invention. In cases where intramuscular injection is the chosen mode of administration, an isotonic formulation is used. Generally, additives for isotonicity can include sodium chloride, dextrose, mannitol, sorbitol and lactose. Isotonic solutions such as phosphate buffered saline may be used. Stabilizers include gelatin and albumin.

DNA-based pharmaceutical agents are being developed as a new generation of vaccines. DNA therapeutics are typically plasmids that contain one or more DNA vaccines are typically plasmids which contain one or more genes from a particular pathogen or undesirable cell. Once injected, the coding sequence of the DNA vaccine is expressed in the patient or vaccinee as protein products and an immune response against the protein product is induced. Examples of protocols for delivering DNA which can be adapted for use with the present invention are described in U.S. Patent No. 5,593,972 issued January 14, 1997 to Weiner, U.S. Patent No. 5,589,466 issued December 14, 1996 to Felgner et al., U.S. Patent

Number 4,945,050 issued July 31, 1990 to Sanford et al., U.S. Patent Number 5,036,006 issued July 30, 1991 to Sanford et al., PCT publication serial number WO 90/11092, PCT publication serial number WO 93/17706, PCT publication serial number WO 93/23552, and PCT publication serial number WO 94/16737 which are each incorporated herein by reference.

In preferred embodiments of the invention, pharmaceutical compositions comprising nucleic acid molecule comprising a nucleotide sequence encoding an attenuated, non-functional *vif* protein is administered to a mammal by the methods described above in order to induce a humoral and/or a cellular immune response to *vif* protein. In other 10 embodiments of the invention, the pharmaceutical compositions of the invention can be co-administered with additional compounds. Such additional compounds include, for example, different viral proteins or nucleic acid molecules encoding a different viral proteins. The different viral proteins include, for example, *gag*, *pol*, *env*, *vpr*, *vpu*, and *tat*, and the like. Such elicited immune responses are protective against HIV or related animal viruses.

The present invention is also directed to antibodies directed against an attenuated, non-functional *vif* protein. As used herein, the term "antibody" is meant to refer to complete, intact antibodies, and Fab fragments and F(ab)₂ fragments thereof. Complete, intact antibodies include monoclonal antibodies such as murine monoclonal antibodies, chimeric antibodies and humanized antibodies. In some embodiments, the antibodies 20 specifically bind to an epitope of *vif* or attenuated, non-functional *vif*. Antibodies that bind to an epitope are useful to isolate and purify that protein from both natural sources or recombinant expression systems using well known techniques such as affinity chromatography. Such antibodies are useful to detect the presence of such protein in a sample and to determine if cells are expressing the protein.

Hybridomas which produce antibodies that bind to *vif* protein, and the 25 antibodies themselves, are useful in the isolation and purification of *vif* and attenuated, non-functional *vif* and protein complexes that include *vif* or attenuated, non-functional *vif*. In addition, antibodies may be specific inhibitors of *vif* activity. Antibodies which specifically bind to *vif* or attenuated, non-functional *vif* may be used to purify the protein from natural 30 sources using well known techniques and readily available starting materials. Such antibodies

may also be used to purify the protein from material present when producing the protein by recombinant DNA methodology.

The production of antibodies and the protein structures of complete, intact antibodies, Fab fragments and F(ab)₂ fragments and the organization of the genetic sequences 5 that encode such molecules are well known and are described, for example, in Harlow, E. and D. Lane (1988) *ANTIBODIES: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. which is incorporated herein by reference. Briefly, for example, *vif* or attenuated, non-functional *vif*, or an immunogenic fragment thereof, is injected into mice. The spleen of the mouse is removed, the spleen cells are isolated and fused with immortalized 10 mouse cells. The hybrid cells, or hybridomas, are cultured and those cells which secrete antibodies are selected. The antibodies are analyzed and, if found to specifically bind to *vif* or attenuated, non-functional *vif*, the hybridoma which produces them is cultured to produce a continuous supply of antibodies.

The present invention is further illustrated by the following examples, which 15 are not intended to be limiting in any way. All references cited in the present application are incorporated in their entirety.

EXAMPLES

Example 1: Patients

Virus from one HIV-1 positive transmitter mother (T1) and one HIV-1 20 positive non-transmitter mother (N1) were used in the present invention. Peripheral blood lymphocytes (PBLs) obtained during the subject's third trimester were provided by the Mother Infant Cohort Study, Viral Epidemiology Branch, NCI (Rockville, MD). A follow up examination was performed on the subjects and their offspring in order to determine transmission status.

25 Example 2: HIV-1 Isolation

Infected primary lymphocytes were co-cultivated with PHA-stimulated normal donor lymphocytes for 2 weeks. Virus production was monitored by: 1) measuring the levels of intracellular HIV-1 reverse transcriptase (RT) (Velpandi, *et al.*, *J. Virol. Meth.*, 1990, 29, 291; incorporated herein by reference) and 2) measuring the amount of HIV-1 p24 antigen

released into the medium using a p24 antigen kit (Coulter Corporation), used according to the manufacturer's guidelines.

Example 3: DNA Preparation And PCR Amplification

High molecular weight (genomic) DNA was prepared from the infected PBLs 5 and amplifies through PCR technology as described in Velpandi, *et al.*, *J. Virol. Meth.*, 1990, 29, 291, incorporated herein by reference. Briefly, the PCR mixture contained 5 to 10 µg of genomic DNA, 50 mM KCl, 2.5 mM MgCl₂, 10 mM Tris/HCl (pH 8.0), 800 µM dNTPs, 2.5 units Taq polymerase, 20 pmol oligonucleotide primers and double de-ionized water (ddH₂O) in a final volume of 100 µl. Reaction temperatures and cycling times were: 94°C-denaturing 10 (1 minute), 55°C-annealing (1.5 minutes) and 72°C-extension (2 minutes). The cycle was repeated 35 times. The primer sequences are as follows: Vif(+) 5'-GAAAGCTTATGGAAAAACAGATGGCAG-3' (5046-5065) (SEQ ID NO:2); and Vif(-) 5'-GCAAAGCTTCATTGTATGGCTC-3' (5609-5626) (SEQ ID NO:3). The primers were tagged with a HindIII restriction site (in bold) for cloning purposes.

15 Example 4: Cloning And Sequencing

PCR-amplified product was used for cloning as described in Velpandi, *et al.*, *DNA Cell Biol.*, 1996, 15, 571, incorporated herein by reference. Plasmid DNA positive for the *vif* gene was purified by mini preparations (Qiagen, CA) and quantitated by spectrophotometry in preparation for sequencing of the insert. Sequencing reactions were 20 performed using an ABT automated sequencer and Dye Deoxy reactions (Applied Biosystems, Foster City, CA).

Example 5: Sequence Analysis

Sequence alignments were constructed using the Genetics Computer Group 25 Sequence Analysis software package acquired through the Medical School Computer Facility of the University of Pennsylvania VAX system. Homology comparisons of amino acid sequences were carried out by sequence alignment programs.

Example 6: Construction Of Vif-Defective Provirus

HIV-1 proviral DNA, pZr6, was used to construct a vif deletion mutant as described in Nagashunmugam, *et al.*, *DNA Cell Biol.*, **1996**, *15*, 353, incorporated herein by reference. The resulting proviral clone, p911, contains an 80 amino acid deletion in the vif gene which does not affect the 3' reading frame. Briefly, HIV-1 proviral DNA pZr6 was derived from primary blood lymphocytes infected with HIV_{Zr6} as described in Srinivasan, *et al.*, *Gene*, **1987**, *52*, 71-82, incorporated herein by reference in its entirety. A deletion was introduced into pZr6 to prepare p911. The mutant was constructed so as not to interfere with the upstream pol gene or the downstream vpr gene. Plasmid pZr6 contains two NdeI sites in 10 the vif gene at nucleotide positions 476 and 716. Srinivasan, *et al.*, *Gene*, **1987**, *52*, 71-82. The NdeI fragment (477-716) was deleted from pZr6 and the ends were religated to construct p911, an in-frame mutant that has 80 amino acids deleted in the central region of the vif protein.

Example 7: Construction Of Vif Expression Vectors

15 The vif expression plasmid, pCVif, contains the vif gene from the well-characterized HIV-1 molecular clone, pHXB2, under the control of the cytomegalovirus (CMV) immediate early promoter, within the backbone plasmid, pRc/CMV (Invitrogen, San Diego, CA) as described in Nagashunmugam, *et al.*, *DNA Cell Biol.*, **1996**, *15*, 353, incorporated herein by reference. The vif genes from the maternal samples were cloned into 20 the Invitrogen expression vector, pCDNA3, under the control of the CMV promoter. The vif reading frames were verified through sequence analysis using the forward primer, T7, and the reverse primer, SP6. Briefly, to construct a vif expression vector (pCVif), an Eco RI-Eco RI 1.1 kb fragment from pHXB2 (map coordinates 4,647-5,742; Ratner, *et al.*, *Nature*, **1985**, *313*, 277-284, incorporated herein by reference in its entirety) was cloned under the control of the 25 cytomegalovirus immediate early promoter into plasmid pCDNA3 obtained from Invitrogen. This fragment also contains flanking sequences from parts of the pol and vpr genes, which are not transcriptionally active as shown in a similar construct by Blanc, *et al.* (*Virology*, **1993**, *193*, 186-192).

Example 8: In Vitro Translation Of Vif

In vitro transcription and translation was performed on 1 µg of *vif* expression construct DNA using T7 RNA polymerase according to the manufacturer's instructions (Promega, Madison, WI). Five (5) µl of the *in vitro* translation reaction products were 5 combined with 500 µl of radioimmunoprecipitation assay buffer and immunoprecipitated with rabbit anti-*vif* antiserum as described. Mahalingam, *et al.*, *Virol.*, 1995, 214, 647.

Example 9: Cells

Rhabdomyosarcoma (RD) cells, obtained from the American Type Culture Collection (ATCC), were grown in a monolayer at 37°C in 5% CO₂ in Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum, 1% penicillin, 1% streptomycin and 1% L-glutamine. Lymphocytoid cell lines obtained from ATCC were maintained as suspension cultures in RPMI 1640 medium, supplemented with 10% fetal bovine serum, penicillin (100 U/ml) and L-glutamine (540 µg/ml) at 37°C with 5% CO₂. Phytohemagglutinin-stimulated (10 µg/ml) PBLs were maintained in RPMI 1640 medium 15 containing 10% T-cell growth factor.

Example 10: Immunization Of Mice With Vif Constructs

For immunization experiments in mice, 3 different *vif* constructs were used. The *vif* clones selected were T-35 (from transmitter), N-15 (from non-transmitter) and pCVif (*vif* gene of HIV-1_{SF-2}). pCDNA3 vector DNA was used as a negative control. In order to 20 enhance DNA uptake, the quadriceps muscles of BALB/c mice were injected with 100 µl of 0.25% bupivacaine 48 hours before DNA injection. Fifty (50) or 100 µg of each *vif* expression plasmid was injected in a final volume of 100 µl into each of 4 mice. The animals were boosted 3 times at two week intervals.

Example 11: ELISA Binding Of Mouse Serum To rvif Protein

ELISA was performed on mouse serum as described in Wang, *et al.*, *AIDS*, 25 1995, 9 (Suppl A), S159. Briefly, ELISA plates were coated with recombinant *vif* (rvif) protein at concentration of 100 ng/well for the binding assays. Mouse sera were diluted (1:100 and 1:500) in blocking buffer, tagged with anti-mouse IgG conjugated to horseradish

peroxidase (HRP) and detected by TMBBlue substrate. The non-specific binding and the prebled sera binding were subtracted from the specific binding of the DNA injected animal sera.

Example 12: CTL Assay Using Vaccinia Expressing *vif*

5 DNA injected mice were sacrificed 7 weeks after the first immunization, and their spleens were removed for CTL and T-cell proliferation assays as described in Wang, *et al.*, *DNA Cell Biol.*, **1993**, *12*, 799. Briefly, P815 cells infected with *vif*-expressing vaccinia (VV:gag kindly provided by NIH AIDS Reagent and Reference Program) were used as target cells. Ten (10) μ Ci of Na_2CrO_4 (^{51}Cr , 534 mCi/mg, Dupont Co.) was added to $1 \times 10^6/\text{ml}$ target cells which were subsequently incubated for 2 hours at room temperature. The cells were then washed 3 times with serum-free media and diluted to a volume of 1×10^5 cells/ml in RPMI 1640/10% calf serum. The effector spleen cells were washed once, resuspended and diluted to a concentration of 1×10^7 cells/ml of RPMI medium. 1:2 serial dilutions were made from this stock cell solution (5×10^6 , 2.5×10^6 and 1.25×10^6 cells/ml). One hundred (100) μl of these effector cell solutions were aliquoted into a 96-well microliter flat bottom plate. One hundred (100) μl of target cell solution was added to each well. The resultant effector to target cell ratios were 100:1, 50:1, 25:1 and 12.5:1. In order to determine the spontaneous or maximum chromium release, respectively, target cells were mixed with either 100 μl of media alone or 1% Triton-X. The effector and target cells were then incubated at 37°C in a 20 5% CO₂ incubator for 5 hours. A 100 μl aliquot of supernatant was removed from each well, and the amount of ^{51}Cr release was measured in a gamma counter. The formula for calculation of the specific CTL release is below: $100 \times [(\text{experimental release} - \text{spontaneous release}) / \text{maximum release} - \text{spontaneous release}]$. Note: maximum release was determined by lysis of target cells in 1% Triton X-100.

25 **Example 13: CTL Assay Using Clinical HIV-1 Isolates**

HeLa CD4+ cells expressing mouse MHC-I were infected with HIV-1 clinical isolates and used as target cells in the CTL assay. The CTL assay was performed as described in Chada, *et al.*, *J. Virol.*, **1993**, *67*, 3409.

Example 14: T Cell Proliferation Assay

- Assays were performed in triplicate. Splenocytes were isolated as discussed above, resuspended in RPMI 1640 and diluted to a concentration of 3.3×10^6 cells/ml. A 150 μ l aliquot was immediately added to each well of a 96-well microtiter flat bottom plate.
- 5 Fifty (50) μ l of protein or peptide was added to each well to final concentrations of 10.0, 1.0 or 0.1 mg/ml. The cells were incubated at 37°C in a 5% CO₂ incubator for 3 days. One (1) μ Ci of tritiated thymidine was added to each well, and the cells were incubated overnight under the same conditions. The cells were harvested using automated cell harvester (Tomtec, Orange, CT) and the amount of incorporated tritiated thymidine was measured in a beta counter.
- 10 In order to ensure that the cells were healthy, 5 mg/ml of PHA was used as a non-specific stimulator in a positive control sample.

Example 15: Transcomplementation Of vif Defective Proviral DNA With vif Genes From Maternal Samples

- RD cells (1×10^6) were co-transfected with 10 μ g of a vif defective proviral clone, p911, and 10 μ g pCVif or vif expression plasmid from transmitter or non-transmitter subjects using lipofectin from Boehringer Mannheim (Indianapolis, IN). The co-transfected cells were washed after an 8 hour incubation and resuspended in DMEM media. Culture supernatant was collected after a 72 hour incubation, centrifuged to remove cell debris, passed through a 0.45 μ m filter, and assayed for p24 production (Coulter Corporation). PBMCs (1
- 15 x 10⁷) were infected with an amount of virus equivalent to 100 ng of p24 antigen. Virus-inoculated cells were incubated for 4-6 hours at 37°C and 5% CO₂, washed 3 times with PBS and resuspended in 10 ml of fresh RPMI 1640. An aliquot of the culture supernatant was collected every 3 days in order to quantitate virus production by measuring the amount of p24 antigen released into the medium.
- 20

Example 16: Characterization Of Viruses Isolated From Patients

The HIV-1 positive transmitter and non-transmitter mothers included in the present invention were selected from an AIDS cohort study. The mother and the non-transmitter mother are referred to as T1 and N1, respectively. The clinical status of the subjects and the replication kinetics of their viral isolates are presented in Table 2.

Uncultured lymphocytes from each subject were used in order to obtain wild-type sequences unmodified by *in vitro* selection conditions. In PBMC co-cultivation assays, T1 viral samples replicated very well in normal donor PBLs; whereas N1 viral samples did not replicate in either primary lymphocytes or macrophages.

5

Table 2

Subject	Clinical Stage	PCR	Virus Coculture in PBMC	Infection in CD4+ Cell Lines
Transmitter	Asymptomatic	+++	+++	+++
Non-Transmitter	Asymptomatic	++	---	---

Example 17: Sequence Variation Of *Vif* Gene In Vivo

- 10 In order to investigate the genetic variability of the *vif* gene in these subjects, ten clones from each subject were sequenced and computer-aligned by degree of homology. The nucleotide sequences were then translated into protein sequences. Deduced amino acid sequences were used in the final comparison, since not all nucleotide sequence changes resulted in amino acid sequence changes. The aligned amino acid sequences from these
 15 patients are shown in Figure 1. Clone numbers with the designations, 'T' and 'N' represent variants isolated from transmitter and non-transmitter mothers, respectively. Sequence alignment revealed that each subject had a unique and highly conserved set of sequences within their virus pool. Most of the nucleotide changes were point mutations which generally resulted in substitutions, versus duplications or insertions, within the protein sequence. Three
 20 clones encoded attenuated proteins. Clone T-42 had a 5 amino acid deletion at its 3' end due to a premature stop codon. Clone N-13 had two stop codons (positions 31 and 41) and clone T-4 had a single stop codon (position 77), each of which was introduced within a set of three nucleotides, keeping the reading frame intact 3' to the mutation. The fact that the majority (17 of 20) of the clones encode full-length sequences suggests that there are few defective *vif*
 25 genes present within these patients' viral pools. It is interesting to note that most of the *vif* point mutations are present in the 5' portion of the gene rather than in the 3' region.

Significant differences were found between clones at positions 20, 27, 31, 36, 37, 45, 60, 74, 127, 136, 140 and 150.

In order to determine the nature and the sequence variation of *vif* gene *in vivo*, we cloned and analyzed *vif* variants present in uncultured PBMCs from HIV-1 positive subjects. Analysis of 20 different *vif* sequences from two subjects (10 from each subject) revealed that *vif* is highly conserved (approximately 90%) within a particular patient at a given time point. Although, Wieland, et al. (*J. Virol.*, 1994, 203, 43) reported that the 3' portion of the *vif* gene is highly variable, the results of the present invention indicate that the 5' portion (aa 20-85) is more variable and the 3' portion is well-conserved. In support of the results herein, previous mutagenesis experiments have shown that the C terminus of *vif* (aa 171 to 192) is essential for stable association of *vif* with membranes. Goncalves, et al., (*J. Virol.*, 1994, 68, 704). Among the 20 sequences we analyzed, only two clones had premature stop codons indicating that 90% of *vif* genes isolated were intact *in vivo*. This result, along, with previously published data, suggests that a complete *vif* gene is essential for viral replication *in vivo*. Gabudza, et al., (*J. Virol.*, 1992, 66, 6489; and Sova, et al., (*J. Virol.*, 1995, 69, 2557).

The 20 deduced *vif* protein sequences from these clones exhibited 75% conservation (25% variation) over the entire (192 aa) length. In particular, two antigenic domains, aa 87-94 (IEWRKKRY) (SEQ ID NO: 24) and aa 172-178 (DRWNKPQ) (SEQ ID NO: 25), recognized by HIV-1 positive sera (Wieland, et al., *AIDS Res. Human Retrovir.*, 1991, 7, 861) are well conserved in all 20 clones. The well-conserved nature of these two regions may be responsible for the cross antigenic properties exhibited by these clones. In addition, a sequence which is conserved in 34/38 lentivirus *vif*, SLQYLA (144-149)(SEQ ID NO: 26) (Oberste, et al., *Virus Genes*, 1992, 6, 95), is also conserved in each of the 20 *vif* clones sequenced in the present invention. In previous studies, computer alignment analyses has shown that amino acids 21 to 30, 103 to 115 and 142 to 150 of *vif* are highly conserved among HIV-1, HIV-2 and SIV. Myers, et al., *Human Retrovir. AIDS*, 1988. Clones analyzed in the present invention, however, were generally conserved sequences within aa 103-115 and aa 142-150, but not within aa 21-30. *Vif* protein has been characterized as a cysteine protease with Cys 114 marking its active site and His 48 considered to be important for activity. Guy,

et al., J. Virol., 1991, 65, 1325. In the sequences of the present invention, Cys 114, as well as Cys 133 (the only other cystine in vif) and His 48, were well conserved.

Phylogenetic tree analysis (data not shown) found 3 major families within the 20 patient clones. Ninety (90%) percent of N-derived clones formed a family and 80% of T-derived clones formed a family while the remaining clones, N-30, T-3 and T-38, exhibited greater diversity and formed a Separate group (data not shown). When distance comparison was performed, intrapatient variation between the transmitter clones was 12%, versus a variation of 10% between non-transmitter clones. The similarity between the subjects' variant clones and the established laboratory molecular clones, HIV_{SF-2}, HIV_{NL43} and HIV_{Z6}, was also evaluated. The subject isolates shared a higher degree of homology with other clones within their transmitter status group than with any of the laboratory-maintained viral isolates. Based upon their sequence variation, 4 clones from each patient were selected for preliminary translation/immunization experiments (see below).

Phylogenetic tree analysis also illustrated that, in spite of intra-patient variation, clones from the transmitter and nontransmitter subjects clustered separately. *In vitro* transcription/translation of 8 constructs (four from each subject) resulted in the expression of a 23 kDa protein, except in the case of clone N-13 which has a premature stop codon. This suggests that the various mutations present in these vif constructs did not affect the expression kinetics and stability of the protein.

20 Example 18: Expression Of Vif Clones

In vitro transcription/translation was performed upon 5 clones from each group in order to assess their levels of vif expression. Results are presented in Fig. 2. The products from the *in vitro* translation reactions were immunoprecipitated with vif antiserum and subjected to gel electrophoresis. pCVif (full length vif from HIV-1 strain SF2) and p911 (*vif* mutant) provirus were used as a positive and negative control, respectively. *In vitro* translation with pCVif and each of the full length *vif* expression plasmids produced a 23 kDa protein; whereas clones p911 and N-13 did not result a protein product of 23 kDa size, probably due to the presence of premature stop codons. Two (2) clones from each subject group were selected for further evaluation, based upon similar serological characteristics (data not shown). The patient clones selected as representatives from each group were T-35 (from

transmitter) and N-15 (from non-transmitter). Each of these clones contain mutations characteristic of their particular group and represent the highest level of diversity within these groups. It is interesting to note that mutations within clone N-15 are dispersed throughout the full length gene; whereas mutations within clone T-35 are clustered at the 5' end of the
5 gene.

Example 19: Induction Of Humoral Responses *In Vivo*

Specific anti-vif immune responses were apparent in sera collected from mice immunized with T-35, N-15 and pCVif expression plasmids, but not in sera from mice immunized by pcDNA3 vector alone. The induction of immune response correlated with

- 10 DNA injection concentration, as well as the number and time interval between boosts. Sera from 4 mice injected with either 50 or 100 µg of vif/DNA had specific reactivity to vif protein when measured by ELISA (Fig. 3). Induction of the humoral response was dose-and time-dependent. Injection of 50 µg of DNA induced an immune response detectable by ELISA at 15 days following the first injection. This response increased after subsequent boosts,
15 reaching a maximum level 45 days after 2 boosts (Panel A). Injection with 100 µg of DNA induced a response that reached a maximum level only 28 days after a single boost (Panel B). In addition, the antibody response can be elevated 219 days after the three injections with a single boost of DNA (data not shown). The level of antibody response varied between vif clones. Most importantly, the non-transmitter clone, N-15, induced a higher serological
20 response than the transmitter clone, T-38, or pCVif. This suggests that non-transmitter vif is capable of inducing a more efficient B-T helper dependent response than transmitter vif in this strain of mice.

Example 20: Induction Of Cellular Responses *In Vivo* Using Vaccinia Expressing Vif

- Four mice, each immunized with one of the vif constructs, were given an
25 additional boost 15 days after first injection. Two mice were subsequently sacrificed and their splenocytes were used in a cytotoxic T cell (CTL) assay. p815 cells infected with vif-expressing vaccinia were used as target cells. Non-specific lysis by splenocytes from vif-DNA immunized and naive mice was measured using p815 cells infected with non-vif-expressing vaccinia as target cells. Specific target lysis is presented in Fig. 4. The level of

specific CTL activity varied between the *vif* constructs. Splenocytes from mice immunized with clone pCVif exhibited 45% lysis at a effector: target ratio of 100:1. Clones T-35 and N-15 exhibited 17 and 12% lysis, respectively, at the same ratio. These results clearly demonstrate that *vif* DNA immunization induces specific CTL responses. The differences 5 in the levels of CTL activity induced by *vif* gene inoculation between the various patient clones may be due to mutations within the CTL epitopes expressed by vaccine targets or differences in immune responsiveness in this haplotype.

Example 21: Evaluation Of Cellular Responses *In Vivo* Using Human Targets Infected With A Clinical HIV-1 Isolate

10 In order to evaluate the ability of the *vif* clones to induce lysis of virally infected targets, we used HIV-1 infectable HeLa CD4/D^d cells which express both the CD4 receptor and the murine class I H-2D^d restriction element, as targets in the CTL assay. These cells were infected with an HIV-1 isolate derived from a symptomatic AIDS patient for 7 days. Figure 5 (A-D) represents CTL assay results. Splenocytes obtained from mice injected 15 with each of the DNA constructs exhibited *vif*-specific lysis. Clones T-35, N-15 and pCVif presented with 27, 26 and 24% lysis, respectively, at an effector:target ratio of 50:1. All three clones exhibited 20% lysis at a ratio of 25:1. This demonstrates that a cellular immune response against native HIV-1 isolates can be generated through genetic vaccination with *vif* expression vectors.

20 **Example 22: Induction Of Antigen Specific T-Cell Proliferation**

Specific T-cell proliferation responses against HIV-1 *vif* protein were also studied in DNA-immunized animals. Lymphocytes from *vif*-immunized mice demonstrated a significant proliferative response against rvif protein. Figure 6 illustrates the proliferation index of different *vif* constructs versus DNA injection concentrations. The results show that 25 the MHC class II-dependent T_h (helper) cell response is dose dependent. For each construct, the stimulation index is almost 2-fold higher in mice injected with 100 µg of *vif*/DNA than in mice injected with 50 µg of *vif* DNA. Comparison of the three different *vif* constructs also indicates that, at each injection concentration, clone T-35 induces a higher stimulation index than either N-15 or pCVif.

Example 23: Transcomplementation of HIV-1 Vif- Proivirus With Vif Expression Plasmids

As expected, transient transfection of RD cells with HIV-1 (*vif*-) proviral DNA and *vif* expression plasmids did not reveal any differences in virus production between T-derived, N-derived or control plasmids (data not shown). Any differences in *vif* function would be demonstrated at the level of new infection. When rescued virus was used to infect primary lymphocytes, however, a significant difference was observed in virus pathogenesis between T- and N-derived and control plasmids (Table 3). The *vif*-negative proviral clone (p911) alone was unable to infect primary PBLs as cell-free virus. When trans-complemented virus (p911 + pCVif) was used to infect the PBLs, infectivity was five-fold less than that of wild-type virus. In contrast, each of the T-derived clones tested were able to rescue the (*vif*-) mutant (approximately 100% positive virus control). However, none of the N-derived clones were able to efficiently infect PBLs as cell-free virus. Therefore, N-15 and similar N-derived clones were able to induce anti-HIV immune responses in mice in the absence of functionality.

Table 3

Samples	DNA Used to Derive Viruses for Infection	Amount of p24 Released (ng/ml)
Proviral Clone	pZr6	101,846
Vif Mutant	p911	60
Vif Mutant + pCVif	p911 + pCVif	22,679
Vif Mutant + Transmitter Clones	p911 + T1-40 p911 + T1-37 p911 + T1-35 p911 + T1-38	21,896 17,230 19,470 81,570
Vif Mutant + Non-Transmitter Clones	p911 + N1-13 p911 + N1-15 p911 + N1-17 p911 + N1-27 p911 + N1-30	520 530 1,090 1,277 715

RD cells were transfected with 10 µg of pZr6, vif mutant p911, p911 and vif expression plasmids from different patient samples. Virus pools were prepared from supernatant collected 72 hours after transfection. Virus equivalent to 100 ng of p24 antigen was subsequently used to infect 10 x 10⁶ PBMCs. Infection was monitored by p24 antigen 5 production.

Example 24: Observations

N-derived clones were attenuated in their ability to transcomplement vif defective HIV-1 provirus. One of the clones analyzed, N-15, was also immunologically functional and capable of generating an immune response against wild-type HIV-1 virus. A 10 non-functional yet immunogenic clone, such as N-15 in the present invention, could be an effective component of a genetic vaccine directed against HIV-1. It has been shown in the present invention that vif alone can generate an effective response against native HIV-1 virus *in vitro*. Such immunogens could be useful in a therapeutic setting to target the immune response against native vif expressing viruses. While it is likely that escape variants can 15 occur viruses expressing defective vifs due to this selection might now exhibit attenuated *in vivo* growth kinetics. In a similar manner a prophylactic vaccine which includes vif could serve to both limit viral escape and contribute to lowering the viral set point during the early infection events.

What is Claimed is:

1. An isolated, attenuated, non-functional *vif* protein.
2. The protein of claim 1 wherein said protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, and SEQ ID NO:23.
3. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an attenuated, non-functional *vif* protein.
4. The nucleic acid molecule of claim 3 wherein said nucleic acid molecule comprises a nucleotide sequence which encodes an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.
5. The nucleic acid molecule of claim 3 wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.
6. A pharmaceutical composition comprising a protein of claim 1 in a pharmaceutically acceptable carrier or diluent.

7. A pharmaceutical composition comprising a nucleic acid molecule of claim
3 in a pharmaceutically acceptable carrier or diluent.

8. A recombinant expression vector comprising a nucleic acid molecule of claim
3.

5 9. The recombinant expression vector of claim 8 wherein said nucleic acid
molecule comprises a nucleotide sequence which encodes an amino acid sequence selected
from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7,
SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID
NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18,
10 SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.

10. A host cell comprising a recombinant expression vector comprising a nucleic
acid molecule of claim 3.

11. The host cell of claim 8 wherein said nucleic acid molecule comprises a
nucleotide sequence which encodes an amino acid sequence selected from the group
15 consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8,
SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID
NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.

12. A purified antibody directed against an attenuated, non-functional *vif* protein.

20 13. The antibody of claim 12 wherein said protein comprises an amino acid
sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,
SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID
NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17,
SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, and SEQ
25 ID NO:23.

14. A method of immunizing a mammal against a virus comprising administering to cells of said mammal, a nucleic acid molecule that comprises a nucleotide sequence that encodes an attenuated, non-functional *vif* protein, wherein said nucleic acid molecule is expressed in said cells.
- 5 15. The method of claim 14 wherein said nucleic acid molecule comprises a nucleotide sequence which encodes an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, 10 SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23.
16. The method of claim 14 wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, 15 SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.
17. The method of claim 14 wherein said virus is selected from the group consisting of human immunodeficiency virus, feline immunodeficiency virus, bovine immunodeficiency virus, Visna virus, and simian immunodeficiency virus.
- 20 18. A plasmid comprising a nucleotide sequence encoding an isolated, attenuated, non-functional *vif* protein.
19. The plasmid of claim 18 wherein said protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, 25 SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, and SEQ ID NO:23.

20. The plasmid of claim 18 wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41,
5 SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45 and SEQ ID NO:46.

1	51	100
N24	-y-	-y-
N27	-y-	-y-
N26	-y-	-y-
N15	-y-	-y-
N17	-y-	-y-
N23	-y-	-y-
N29	-y-	-y-
N13	-y-	-y-
N22	-y-q-e-n-h-	-y-q-e-n-h-
T39	-a-	-a-
T44	-a-	-a-
T43	-a-	-a-
T37	-e-a-	-e-a-
T40	-e-a-	-e-a-
T35	-a-	-a-
T4	-a-	-a-
T3	-a-	-a-
T38	-a-	-a-
T42	-a-	-a-
Con	Menyantri Moderate Insurah Vektor-Wet Rhinseptu Visenwihig Darleutin Ghi-Geroh Logastear Krestumop	
101	151	194
N24	-h-----	-h-----
N27	-h-----	-h-----
N26	-h-----	-h-----
N15	-h-----	-h-----
N17	-h-----	-h-----
N23	-h-----	-h-----
N29	-h-----	-h-----
N13	-h-----	-h-----
N22	-h-----	-h-----
T39	-h-----	-h-----
T44	-h-----	-h-----
T43	-g-----	-g-----
T37	-e-----	-e-----
T40	-e-----	-e-----
T35	-e-----	-e-----
T4	-e-----	-e-----
T3	-v-----	-v-----
T38	-v-----	-v-----
T42	-v-----	-v-----
Con	Liaquiajy Yedosessal Roollgrvs Preyongan Kostional Aalitrik Pelsugit Efrankoot Keris-Him Ngi	

FIGURE 1

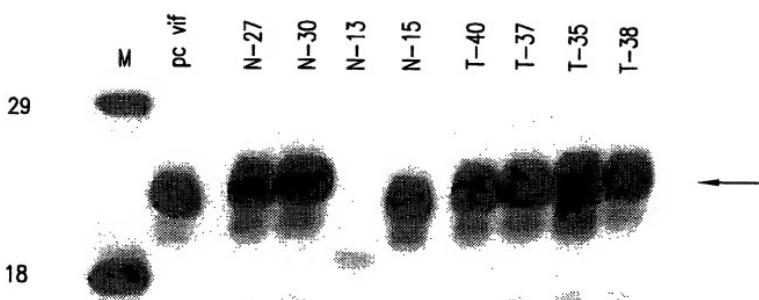


FIG.2

FIGURE 3B

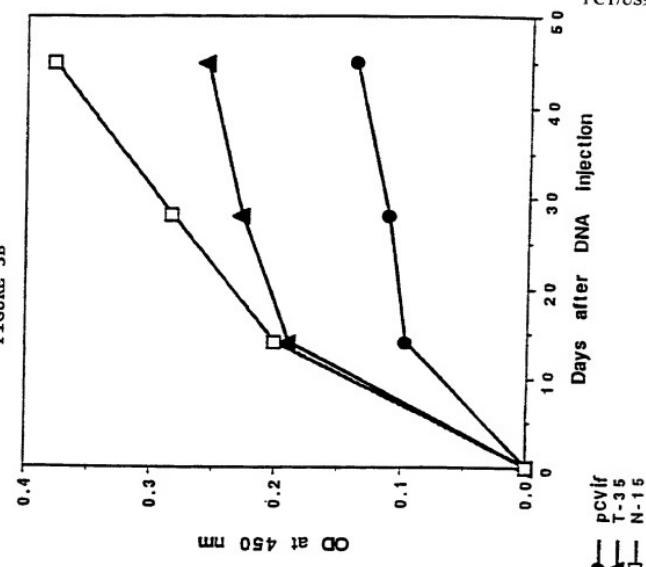
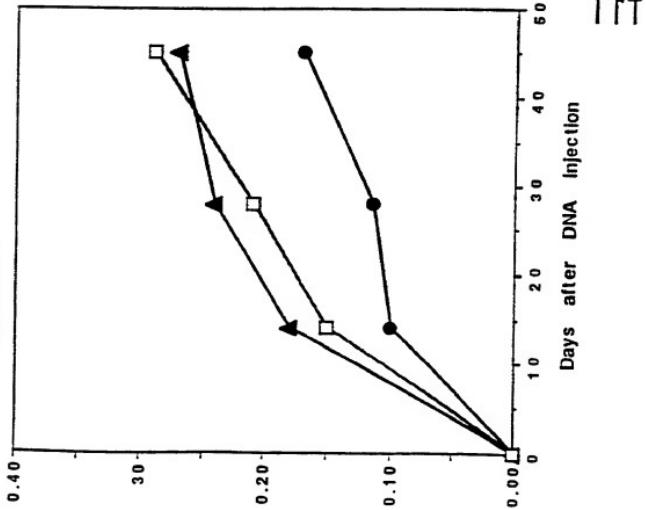


FIGURE 3A



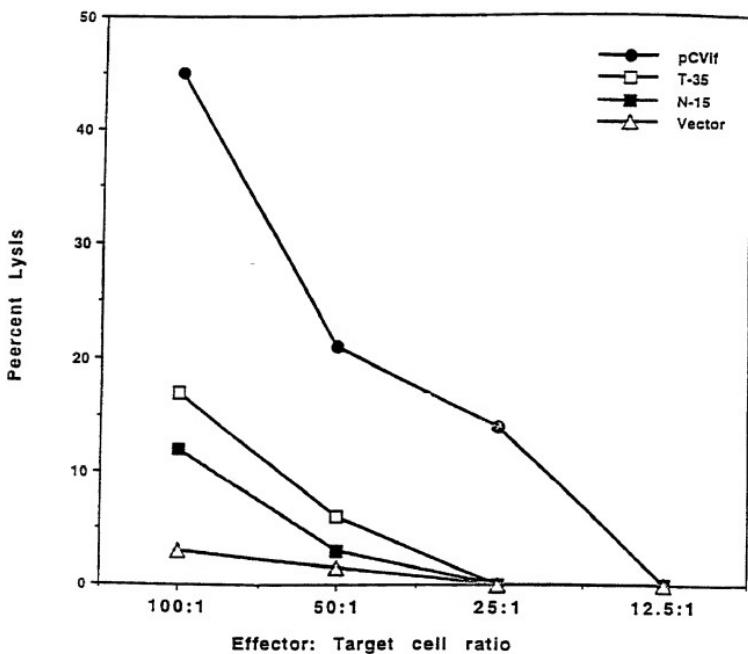
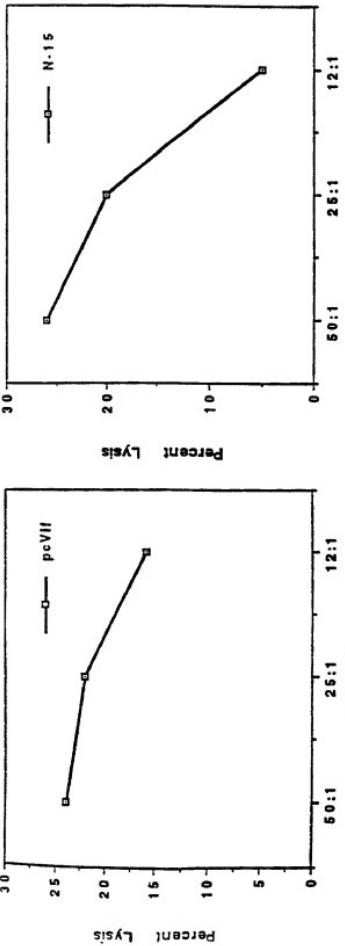
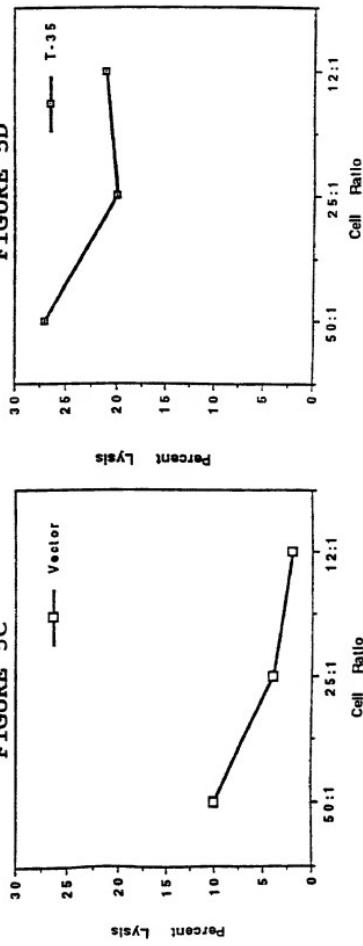
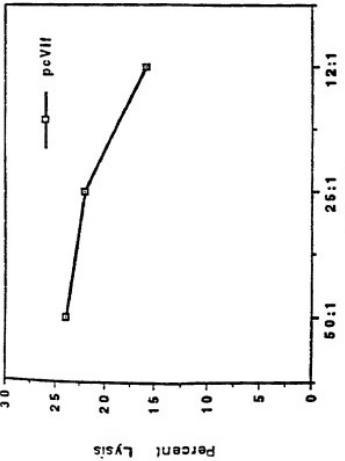
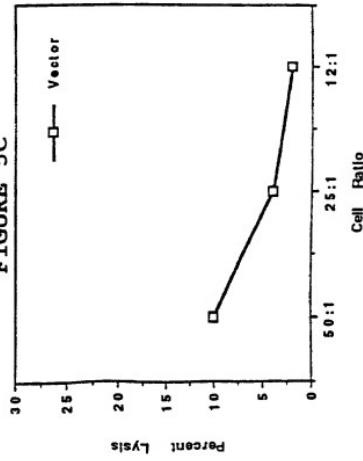


FIGURE 4

FIGURE 5B**FIGURE 5D****FIGURE 5A****FIGURE 5C**

T-cell proliferation

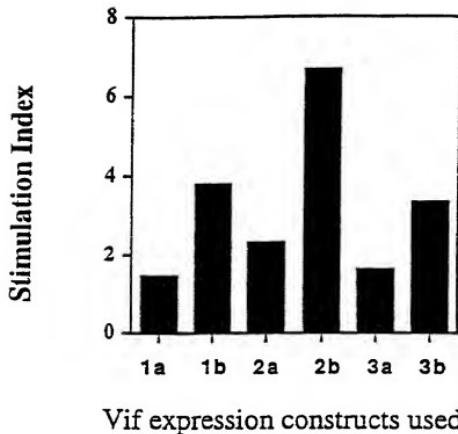


FIGURE 6

FIGURE 7A**1. Vif-N13.pep**

MENRQVIIIV WQVDRMRIRT WNSLVKYHMY *SKKAREWFY *HHYQSPHPK
VSSEVHIPLE DARLEITTSFW GLHTGERDWH LGQGVSIERW KRRYSTHVDP
DLADQLIHLHY YFDCFSESAII RKAIIGLHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLASVRKLT EDRANKPQKT KGHRGSHIMN GH*

2. Vif-N15.pep

MENRQVMIV WQVDRMRIRT WNSLVKYHMY RSKKAREWFY RHHYQSPHPR
VSSEVHIPLE DARLEITTYW GLHTGERDWH LGQGVSIERW KRRYSTQVDP
DLADQLIHLHY YFDCFSESAII RKAIIGLHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EDRANKPQKT KGHRGSHIMN GH*

3. Vif-N17.pep

MENRQVMIV WQVDRMRIRT WNSLVKYHMY RSKKAREWFY RHHYQSPHPK
VSSEVHIPLE DARLEITTYW GLHTGERDWH LGQGVSIERW KRRYSTQVDP
DLADQLIHLHY YFDCFSESAII RKAIIGLHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EDRANKPQKT KGHRGSHIMN GH*

FIGURE 7B

4. Vif-N22.pep

MENRWQVMIV WQVDRMRIRT WNSLVITYHMY RSQKAREWFN RHHYQSPHPK
VSSEVHIPLE DARLAIPTFW GLHTGERDWH LGQGVSIERW KRRYSTQVDP
DLADQLIHLHY YFDCFSSESAI RKAILGHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EIDWANKPQKT KGHRGSHIMN GH*

5. Vif-N24.Pep

MENRWQVMIV WQVDRMRIRT WNSLVKYHMY RSKKAREWFY RHHYQSPHPK
VSSEVHIPLE DARLVITTYW GLHTGERDWH LGQGVSIERW KRRYSTIHVDP
DLADQLIHLHY YFDCFSSESAI RKAILGHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLASVRKLT EIDWANKPQKT KGHRGSHIMN GH*

6. Vif-N26.pep

MENRWQVMIV WQVDRMRIRT WNSLVKYHMY RSKKAREWFY RHHYQSPHPK
VSSEVHIPLE DARLVITTYW GLHTGERDWH LGQGVSIERW KRRYSTQVDP
DLADQLIHLHY YFDCFSSESAI RKAILGHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLASVRKLT EIDWANKPQKT KGHRGSHIMN GH*

7. Vif-N27.pep

MENRWQVMIV WQVDRMRIRT WNSLVKYHMY RSKKAREWFY RHHYQSPHPK
VSSEVHIPLE DARLVITTFW GLHTGERDWH LGQGVSIERW KRRYSTIHVDP
DLADQLIHLHY YFDCFSSESAI RKAILGHRVS PRCEYRAGHS KVGSLOYLAI

FIGURE 7C

AALITPKKIK PPLPSVRKLT EDRWNPQKT KHRGSHIMN GH*

8. Vif-N29.pep

MENRWQVMIV WQVDRMRIRT WNSLVVKHMY RSKKAREWFN RHHYHRPHPK
VSSEVHIPLE DARLEITTIFW GLHTGERDWH LGQGVSTIEWR KRRYSTQVDP
DLADQLIHLHY YFDCFSESAl RKAIIGLHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EDRWNPQKT KHRGSHIMN GH*

9. Vif-N30.

MENRWQVMIV WQVDRMRIRT WNSLVVKHMY RSQKEREWFN RHHYHSPHE
QSSTAHIPLV DGRLEKIAWW SLDTIGEGWHL RGHRVSTIEWR KRRYSTQVDP
DLVDQLIHLHY YFDCFSESAl RKAIIGLHRVS PRCEYRAGHS KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EDRWNPQKT KHRGSHIMN GH*

Vif-T3.pep

MENRWQVMIV WQVDRMRIRT WNSLVKHHMY VSKKAKKWFY RHHYESPHPK
VSSTAHIPLG DGRLEKIAWW SLOAGDGWHL RGHPVSTIEWR KRRYSTQVDP
DLVDQLIHLHY YFDCFSESAl RKAIIGYRVS PRCEYQAGHN KVGSLOYLAI
AALITPKKIK PPLPSVRKLT EDRWNPQKT KHRGSHIMN GH*

Vif-T35.pep

FIGURE 7D

MENRWQVMIV WQVDRMRIRA WNSLVKHHIY FSKKAKKWFY RHHYESPHEN
 VSSEVHPLG DARLVITPYW GLHAGERDWY LAQGVSIWR KRRYSTQVDP
 DLADQLIHLY YFDCFSESAII RKAIIIGYRVS PRCEYQAGHN KVGSLOYAL
 AALITPKKIK PPLPSVRKLIT EIDRANKPQKT KGHRCGSHMN GH*

Vif-T37.pep

MENRWEVMIV WEVDRMRIRA WNSLVKHHMY VSKKAKKWFY RHHYESPHPK
 VSSEVHPLG DARLVITTYW GLHAGERDWH LGQGVSIWR KRRYSTQVDP
 DLADQLIHLY YFDCFSESAII RKAIIIGYRVS PRCEYQAGHN KVGSLOYAL
 AALITPKKIK PPLPSVRKLIT EIDRANKPQKT KGHRCGSHMN GH*

Vif-T38.pep

MENRWQVMIV WQVDRMRIRA WNSLVKHHMY VSKNAKKWFY RHHYDSPHEV
 QSSTAHIPLG DGRLOKIAFW SLDAGERDWL LGQGVSIWR KRRYSTQVDP
 DLADQLIHLY YFDCFSESAII RKAIIIGYRVS PRCEYQAGHN KVGSLOYAL
 AALITPKKIK PPLPSVRKLIT EIDRANKPQKT KGHRCGSHMN GH*

Vif-T39.pep

MENRWQVMIV WQVDRMRIRA WNSLVKHHMY VSKKAKKWFY RHHYDSPHEPK
 VSSEVHPLG DARLEITTYW GLHAGERDWL LGQGVSIWR KRRYSTIHVDP

FIGURE 7E

DLADQLIHL YFDCFSESA RKAIIIGYRVS PRCEYQAGHN KVGSLOYLAL
 AALITPKKIK PPLPSVRKL T EDWANKPQKT KGHRGSHIMN GH*

Vif-T4.pep

MENRWQVMIV WQVDRMRIR A WNSLVKHHMY VSKKARIWFS RHHYGSHPK
 VSSEVHPILG DARLVITTYW SLHAGE*DWH VQGRVSIEWR KRRYSTQVDP
 DLADQLIHL YFDCFSESA RKAIIIGYRVS PRCEYQAGHN KVGSLOYLAL
 AALITPKKIK PPLPSVRKL T EDWANKPQKT KGHRGSHIMN GH*

Vif-T40.pep

MENRWQVMIV WQVDRMRIR A WNSLVKHHMY VSKKAKKWFY RHHYESHPK
 VSSEVHPILG DARLVITTYW GLHAGERDWH LGQGVSIER KRRYSTQVDP
 DLADQLIHL YFDCFSESA RKAIIIGYRVS PRCEYQAGHN KVGSLOYLAL
 AALITPKKIK PPLPSVRKL T EDWANKPQKT KGHRGSHIMN GH*

Vif-T42.pep

MENRWQVMIV WQVDRMRIR A WNSLVKHHMY VSKKAKKWFN RHHYDRPHPK
 VSSEVHPILG DARLEITTFW GLHAGERDWH LGQGVSIER KRRYSTQVDP
 DLADQLIHL YFDCFSESA RKAIIIGYRVS PRCEYQAGHN KVGSLOYLAL
 AALITPKKIK PPLPSVRKL T EDWANKPQKT KGTEGAIQ*

FIGURE 7F

Vif-T43.pep

MENRWQVMIV WQVDRMRIRA WNSLVKHHMF VSKKAKKKWFY RHHYESPHPK
VSSEVHPLG DARLETTIFW GLHAGERDWH LGQGVSIWR KRRYSTQVDP
DLADQLIHLHY YFGCFSESAL RKAILGYRVS PRCEYQAGHN KVGSLOQYLGL
AALITPKKIK PPLPSVRKLT EIRWNPQKT KHRGSHIMN GR*

Vif-T44.pep

MENRWQVMIV WQVDRMRIRA WNSLVKHHMY VSKKAKKKWFY RHHYESPHQ
VSSEVHPLG DARLETTIYW GLHAGERDWH LGQGVSIWR KRRYSTQVDP
DLADQLIHLHY YFDCFSESAL RKAILGYRVS PRCEYQAGHN KVGSLOQYLAL
AALITPKKIK PPLPSVRKLT EIRWNPQKT KHRGSHIMN GR*

12/17

FIGURE 8A

N13 (SEQ ID NO:27)

ATGGAAAACAGATGGCAGGTGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAAC
 TGGAACAGTTAGTAAATACCATATGTATGTCAAAGAACGCTAGGGATGGTTTAT
 TGACATCACTATCAAAGTCTCATCCAAAAGTAAGTTCAGAAGTACACATCCCCTAGAG
 GATGCTAGATTGAAATAACATCATTTGGGGTCTGCATAACAGGAGAACAGAGACTGGCAT
 TTGGGTCAGGGAGTCTCCATAGAATGGAGGAAGAGGATATAGCACACAGTCGACCC
 GATCTAGCAGACCAACTAATTCTGTATTATTTGATTGTTTCAAGAACATCTGTCTATA
 AGAAAAGCCATATTAGGCACACAGTTAGTCTAGGTGAAATATCGAGCAGGACATAGC
 AAGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAGATAAAG
 CCACCTTGGCGAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACACC
 AAGGCCACAGAGGGAGCCATAATGAATGGACACTAG

N15 (SEQ ID NO:28)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAAC
 TGGAACAGTTAGTAAATACCATATGTATAGTCAAAGAACGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCTCATCCAAAAGTAAGTTCAGAAGTACACATCCCCTAGAG
 GATGCTAGATTGAAATAACACATATTGGGGTCTGCATAACAGGAGAACAGAGACTGGCAT
 TTGGGTCAGGGAGTCTCCATAGAATGGAGGAAGAGGATATAGCACACAGTAGACCC
 GATCTAGCAGACCAACTAATTCTGTATTATTTGATTGTTTCAAGAACATCTGTCTATA
 AGAAAAGCCATATTAGGCACACAGTTAGTCTAGGTGAAATATCGAGCAGGACATAGC
 AAGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAGATAAAG
 CCACCTTGGCGAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACACC
 AAGGCCACAGAGGGAGCCATAATGAATGGACACTAG

N17 (SEQ ID NO:29)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAAC
 TGGAACAGTTAGTAAATACCATATGTATAGTCAAAGAACGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCTCATCCAAAAGTAAGTTCAGAAGTCCACATCCCCTAGAG
 GATGCTAGATTGAAATAACACATATTGGGGTCTGCATAACAGGAGAACAGAGACTGGCAT
 TTGGGTCAGGGAGTCTCCATAGAATGGAGGAAGAGGATATAGCACACAGTAGACCC
 GATCTAGCAGACCAACTAATTCTGTATTATTTGATTGTTTCAAGAACATCTGTCTATA
 AGAAAAGCCATATTAGGCACACAGTTAGTCTAGGTGAAATATCGAGCAGGACATAGC
 AAGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAGATAAAG
 CCACCTTGGCGAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACACC
 AAGGCCACAGAGGGAGCCATAATGAATGGACACTAG

N22 (SEQ ID NO:30)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAAC
 TGGAACAGTTAGTAAACATACCATATGTATAGTCAAAGAACGCTAGGGATGGTTTAT
 AGACATCACTATCACAGTCTCATCCAAAAGTAAGTTCAGAAGTCCACATCCCCTAGAG
 GATGCTAGATTGCAATAACACATATTGGGGTCTGCATAACAGGAGAACAGAGACTGGCAT
 TTGGGTCAGGGAGTCTCCATAGAATGGAGGAAGAGGATATAGCACACAGTAGACCC
 GATCTAGCAGACCAACTAATTCTGTATTATTTGATTGTTTCAAGAACATCTGTCTATA
 AGAAAAGCCATATTAGGCACACAGTTAGTCTAGGTGAAATATCGAGCAGGACATAGC
 AAGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAGATAAAG
 CCACCTTGGCGAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACACC
 AAGGCCACAGAGGGAGCCATAATGAATGGACACTAG

FIGURE 8B

N23 (SEQ ID NO:31)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAACAA
 TGGAAACAGTTAGTAAACATATGTATAGATCAAAGAAAGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCCTCATCCAAAAGTAAGTTCAAGAGTACACATCCCACTAGAG
 GATGCTAGATTGGAATAACACATATTGGGGTCTGCATACAGGGAAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGGAGAAAAGGAGATATAGCACACAGCTGCGACCT
 GATCTCGAGACACCACTTAATTCTATCTGTATTATTTGATTGTTTCAGAACTGCTATA
 AGAAAAGCCATATTAGGACACAGAGTTAGTCTTAGGTGAAATATCGAGCAGGACATAGC
 AAGGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAAGATAAAG
 CCACCTTGCGAGTGTCAAGGAAACTGACAGAGGGATAGATGGAACAAGCCCCAGAACAGCC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

N24 (SEQ ID NO:32)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAACAA
 TGGAAACAGTTAGTAAACATATGTATAGATCAAAGAAAGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCCTCATCCAAAAGTAAGTTCAAGAGTACACATCCCACTAGAG
 GATGCTAGATTGGAATAACACATATTGGGGTCTGCATACAGGGAAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGGAGAAAAGGAGATATAGCACACAGCTGCGACCT
 GATCTAGCAGACCAACTAATTCTATCTGTATTATTTGATTGTTTCAGAACTGCTATA
 AGAAAAGCCATATTAGGACACAGAGTTAGTCTTAGGTGAAATATCGAGCAGGACATAGC
 AAGGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAAGATAAAG
 CCACCTTGCGAGTGTCAAGGAAACTGACAGAGGGATAGATGGAACAAGCCCCAGAACAGCC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

N26 (SEQ ID NO:33)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAACAA
 TGGAAACAGTTAGTAAACATATGTATAGATCAAAGAAAGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCCTCATCCAAAAGTAAGTTCAAGAGTACACATCCCACTAGAG
 GATGCTAGATTGGAATAACACATATTGGGGTCTGCATACAGGGAAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGGAGAAAAGGAGATAGCACACAGCTGCGACCT
 GATCTAGCAGACACCACTTAATTCTATCTGTATTATTTGATTGTTTCAGAACTGCTATA
 AGAAAAGCCATATTAGGACACAGAGTTAGTCTTAGGTGAAATATCGAGCAGGACATAGC
 AAGGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAAGATAAAG
 CCACCTTGCGAGTGTCAAGGAAACTGACAGAGGGATAGATGGAACAAGCCCCAGAACAGCC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

N27 (SEQ ID NO:34)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGGCAGGTAGACAGGGATGAGGATTAGAACAA
 TGGAAACAGTTAGTAAACATATGTATAGATCAAAGAAAGCTAGGGATGGTTTAT
 AGACATCACTATCAAAGTCCTCATCCAAAAGTAAGTTCAAGAGTACACATCCCACTAGAG
 GATGCTAGATTGGAATAACACATATTGGGGTCTGCATACAGGGAAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGGAGAAAAGGAGATATAGCACACAGCTGCGACCT
 GATCTAGCAGACACCACTTAATTCTATCTGTATTATTTGATTGTTTCAGAACTGCTATA
 AGAAAAGCCATATTAGGACACAGAGTTAGTCTTAGGTGAAATATCGAGCAGGACATAGC
 AAGGTAGGATCACTACAGTACTTGGCAATAGCAGCATTAAACACCAAAAAAGATAAAG
 CCACCTTGCGAGTGTCAAGGAAACTGACAGAGGGATAGATGGAACAAGCCCCAGAACAGCC
 AAGGTACAGAGGGAGCCATACAATGAATGGACACTAG

FIGURE 8C

N29 (SEQ ID NO:35)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAGGTAGACAGGATGAGGATTAGAAC
 TGGAAACAGTTTGTAAACCATATGTATGATCAAAGAAAAGAAAGGGATGGTAAAT
 AGACATCACTATCACCGCTCTCATCCAAAAGTAAGTTCAAAGACTAGGCATAGAG
 GATCTAGATTGGAAATAACAAACATTGGGGTCTGCATACAGGAGAAAGAGACTGGCAT
 TTGGCTCAGGGAGTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAGTAGCC
 GATCTAGCAGACCAACTAATTCTGTATTATTTTGTGATTTTCAGAAATCTGCTATA
 AGAAAAGCCATTAGGACACAGAGTTAGTCTAGGTGTGAATATCGAGCAGGACATAGC
 AAGGTTAGGACTACAGTACTTGGCAATGAGCAGCTTAATAACACCAAAAAGATAAAG
 CCACCTTGGCAGGTGTCAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

N30 (SEQ ID NO:36)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAGGTAGACAGGATGAGGATTAGAAC
 TGGAAACAGTTTGTAAACCATATGTATGATCAAAGAAAAGAAAGGGATGGT
 TTATAGAGCATACTATCACCGCTCTCATCCAAAAGTAAGTTCAAAGCCACATCCGC
 TAGTGGATGGTAGTTGGAAAAAAATAGCAGTTGGAGTCTGGATACAGGAGATGGCGTCT
 GGCACAGGGGAGCATCGAGTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAGTAG
 ACCCTGTACTAGAGCAGCAACTAATTCTGTATTATTTGATTTCTAGAACATCTG
 CTATAAGAAAAGCCATTAGGACACAGAGTTAGTCTAGGTGTGAATATCGAGCAGGAC
 ATAGCAAGGTTAGGACTACAGTACTTGGCAATAGCAGCTTAATAACACCAAAAAGA
 TAAAGCCACCTTGGCAGGTGTCAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGA
 AGACCAAGGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

T3 (SEQ ID NO:37)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAAGTAGACAGGATGAGGATTAGAAC
 TGGAAACAGTTTGTAAACCATATGTATGTTCAAAGAAAAGCTAAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAAAGTAAGTTCAAACAGCCACATCCGCAGGG
 GATGGTAGATTGGAGAAAACAGCAGTTGGAGTCTGCAGGGAGATGGAGCTGGCAC
 AGGGGCATCCACTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAGTAGACCC
 GATTTGGTAGACCAACTAATTCTGTATTATTTGATTTCTAGAACATCTGCTATA
 AGAAAAGCCATTAGGATATAGGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCTTAATAACACCAAAAAGATAAAG
 CCACCTTGGCCTAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

T4 (SEQ ID NO:38)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAAGTAGACAGGATGAGGATTAGAGCA
 TGGAAACAGTTTACCAACCATATGTATGTTCAAAGAAAAGCTAGGACATGGTTTCT
 AGACATCACTATGGAGCCCTCATCCAAAAGTAAGTTCAAAGACTAGGACATCCACTAGGG
 GATGCTAGATTGGTAGAACACATATTGGAGTCTGCAGGGAGATGGAGACTGGCAT
 GTGGCTCAGAGACTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAGTAGACCC
 GACTTGGCAGACCAACTAATTCTGTATTATTTGATTTCTAGAACATCTGCTATA
 AGAAAAGCCATTAGGATATAGGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCTTAATAACACCAAAAAGATAAAG
 CCACCTTGGCCTAGTGTAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

FIGURE 8D

T35 (SEQ ID NO:39)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAAGTAGACAGGATGAGGATTAGAGCA
 TGGACAGCTTAGTAAACACCATATTCTCAAAGAACGTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAACGTAAGTTCAGAAGTACACATCCCCTAGGG
 GATGCTAGATTGGTGACAACACCATATTGGGGTCTGCATGGAGGAGAAAGAGACTGGTAT
 CTGGCTAGGGAGTCTCCATAGAATGGAGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATTCTGTATTATTGGTATTGTTTCAGAATCTGCTATA
 AGAAAAGCCATATTAGGATATAGAGTTAGCTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTAGGATCTCTACAGTACTTGGCACTAGCAGCATTAAATAACACCAAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

T37 (SEQ ID NO:40)

ATGGAAAACAGATGGGAGGTGATGATTGTGCGGAAGTAGACAGGATGAGGATTAGAGCA
 TGGACAGCTTAGTAAACACCATATGTATGTTCAAAGAACGTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAACGTAAGTTCAGAAGTACACATCCCCTAGGG
 GATGCTAGATTGGTGATAACACCATATTGGGGTCTGCATGCAGGAGAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGAGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATTCTGTATTATTGGTATTGTTTCAGAATCTGCTATA
 AGAAAAGCCATATTAGGATATAGAGTTAGCTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTAGGATCTCTACAGTACTTGGCACTAGCAGCATTAAATAACACCAAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

T38 (SEQ ID NO:41)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAAGTAGACAGGATGAGGATTAGAGCA
 TGGACAGCTTAGTAAACACCATATGTATGTTCAAAGAACGTAAGAAATGGTTTAT
 CGACATCACTATGACAGCCCTCATCCAGTCCAAGTCAACAGCCCACATCCCGCTAGGG
 GATGCTAGATTGGCAGAAAATAGCATTTGGAGTCTGGATGCAGGAGAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGAGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATTCTGTATTATTGGTATTGTTTCAGAATCTGCTATA
 AGAAAAGCCATATTAGGATATAGAGTTAGCTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTAGGATCTCTACAGTACTTGGCACTAGCAGCATTAAATAACACCAAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

T39 (SEQ ID NO:42)

ATGGAAAACAGATGGCAGGTGATGATTGTGCGCAAGTAGACAGGATGAGGATTAGAGCA
 TGGACAGCTTAGTAAACACCATATGTATGTTCAAAGAACGTAAGAAATGGTTTAT
 AGACATCACTATGACAGCCCTCATCCAAACGTAAGTTCAGAAGTACACATCCCCTAGGG
 GATGCTAGATTGGAGATAACACCATATTGGGGTCTGCATGCAGGAGAAAGAGACTGGCAT
 TTGGGTAGGGAGTCTCCATAGAATGGAGAAAAGGAGATATAGCACACAGCTAGACCCCT
 GACCTGGCAGACCAACTAATTCTGTATTATTGGTATTGTTTCAGAATCTGCTATA
 AGAAAAGCCATATTAGGATATAGAGTTAGCTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTAGGATCTCTACAGTACTTGGCACTAGCAGCATTAAATAACACCAAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAACGACC
 AAGGCCACAGAGGGAGCCATACAATGAATGGACACTAG

FIGURE 8E

T40 (SEQ ID NO:43)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGCCAAGTAGACAGGGATGACGATTAGAGCA
 TGGAACAGTTAGTAAACACCATACTGATGTTCAAGAAAAGCTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAAAGTAAGTTCAGAAGTACACATCCACTAGGG
 GATGCTAGATTGGTGTATAACAACATATTGGGCTCTGCATGCAGGAGAAAAGAGACTGGCAT
 TTGGGTCAAGGGACTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACTTGGCAGACCAACTAATCTGTATTATTGTATTGTTTCAAGATCTGCTATA
 AGAAAAGCCATATTAGGATATAGAGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCATTAAACACCAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACATGAATGGACACTAG

T42 (SEQ ID NO:44)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGCCAAGTAGACAGGGATGAGGATTAGAGCA
 TGGAACAGTTAGTAAACACCATACTGATGTTCAAGAAAAGCTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAAAGTAAGTTCAGAAGTACACATCCACTAGGG
 GATGCTAGATTGGAGATAACAACATTTGGGCTCTGCATGCAGGAGAAAAGAGACTGGCAT
 TTGGGTCAAGGGAGTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATCTGTATTATTGGGTTCTGATGCAGGAGAAAAGAGACTGGCAT
 AGAAAAGCCATATTAGGATATAGAGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCATTAAACACCAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACATGAATGGACACTAG

T43 (SEQ ID NO:45)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGCCAAGTAGACAGGGATGAGGATTAGAGCA
 TGGAACAGTTAGTAAACACCATACTGATGTTCAAGAAAAGCTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAAAGTAAGTTCAGAAGTACACATCCACTAGGG
 GATGCTAGATTGGAGATAACAACATTTGGGCTCTGCATGCAGGAGAAAAGAGACTGGCAT
 TTGGGTCAAGGGAGTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATCTGTATTATTGGGTTCTGATGCAGGAGAAAAGAGACTGGCAT
 AGAAAAGCCATATTAGGATATAGAGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCATTAAACACCAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACATGAATGGACACTAG

T44 (SEQ ID NO:46)

ATGGAAAACAGATGGCAGGTGATGATTGTGTGCCAAGTAGACAGGGATGAGGATTAGAGCA
 TGGAACAGTTAGTAAACACCATACTGATGTTCAAGAAAAGCTAAGAAATGGTTTAT
 AGACATCACTATGAAAGCCCTCATCCAAAAGTAAGTTCAGAAGTACACATCCACTAGGG
 GATGCTAGATTGGAGATAACAACATTTGGGCTCTGCATGCAGGAGAAAAGAGACTGGCAT
 TTGGGTCAAGGGAGTCTCCATAGAATGGAGGAAAAGGAGATATAGCACACAAAGTAGACCCCT
 GACCTGGCAGACCAACTAATCTGTATTATTGGGTTCTGATGCAGGAGAAAAGAGACTGGCAT
 AGAAAAGCCATATTAGGATATAGAGTTAGTCTAGGTGTGAATACCAAGCAGGACATAAT
 AAGGTTAGGATCTCACAGTACTTGGCACTAGCAGCATTAAACACCAAAGAAGATAAAG
 CCACCTTGGCTAGTGTGAGGAACTGACAGAGGATAGATGGAACAAGCCCCAGAAGACC
 AAGGCCACAGAGGGAGCCATACATGAATGGACACTAG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Velpandi AYYAVOO;
Thanadavarayan NAGASHUNMUGAM and David
B. WEINER

International Patent Application No.
PCT/US98/19478

International Filing Date: 18 September 1998

U.S. Serial No. 09/486625

Filing Date: 18 September 1998

For:
**ATTENUATED VIF DNA IMMUNIZATION
CASSETTES FOR GENETIC VACCINES**

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and

I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a

Utility Patent Design Patent

is sought on the invention, whose title appears above, the specification of which:

was filed on September 18, 1998 in the PCT/US/RO under
International Serial No. PCT/US98/19478.
 said application having been amended on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to the patentability of this application in accordance with 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a-d) of any **foreign application(s)** for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of any application on which priority is claimed:

Priority Claimed (If X'd)	Country	Serial Number	Date Filed
<input type="checkbox"/>			

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Serial Number	Date Filed	Patented/Pending/Abandoned

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

Serial Number	Date Filed
60/059,283	September 18, 1997
60/060,172	September 26, 1997

I hereby appoint the following persons of the firm of **WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP**, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103 as attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Mark DeLuca	Reg. No.	33,229
Paul K. Legaard	Reg. No.	38,534

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

U.S. APPLICATION NO. (if known see 37 C.F.R. 1.5)

09/486625

INTERNATIONAL APPLICATION NO.
PCT/US98/19478INTERNATIONAL FILING DATE
18 September 1998PRIORITY DATE CLAIMED (earliest)
18 September 1997TITLE OF INVENTION
ATTENUATED VIF DNA IMMUNIZATION CASSETTES FOR GENETIC VACCINESAPPLICANT(S) FOR DO/EO/US
Velpani AYYAVOO; Thanadavarayan NAGASHUNMUGAM and David B. WEINER

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. has been transmitted by the International Bureau.
 - c. is not required, as the application was filed in the United States Receiving Office (RO/US)
 - d. — A translation of the International Application into English (35 U.S.C. 371(c)(2)).
6. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. have been transmitted by the International Bureau.
 - c. have not been made; however, the time limit for making such amendments has NOT expired.
 - d. have not been made and will not be made.
7. — A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
8. — An oath or declaration of the inventor(s) 35 U.S.C. 371(c)(4).
9. — A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
10. — Items 11. to 16. below concern other document(s) or information included:
 11. An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
 12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
 13. A **FIRST** preliminary amendment.
 A **SECOND** or **SUBSEQUENT** preliminary amendment.
 14. A substitute specification.
 15. A change of power of attorney and/or address letter.
 16. Other items or information:
 - A copy of the Published PCT application, including the Search Report.
 - A copy of the International Preliminary Examination Report.
 - A sequence listing in computer readable form.

EXPRESS MAIL Mailing Label No. EL531430471US

Date of Deposit: February 29, 2000

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

MAILER Shelly McKnightSIGNATURE Shelly McKnight

U.S. APPLICATION NO. (Serial No. 7-14947-15)
097486625INTERNATIONAL APPLICATION NO.
PCT/US98/19478ATTORNEY DOCKET NUMBER
UPAP-0287

17. <input checked="" type="checkbox"/>	The following fees are submitted:			CALCULATIONS	PTO USE ONLY
	Basic National Fee (37 CFR 1.492(a)(1)-(5)): \$930.00 Search Report has been prepared by the EPO or JPO.				
	International preliminary examination fee paid to USPTO (37 CFR 1.482) \$720.00 No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(e)(2)) \$790.00				
	Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$1,070.00				
	International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) \$98.00				
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$ 98.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <u>20</u> - 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$	
Claims	Number Filed	Number Extra	Rate		
Total claims	20 - 20 =	0	X \$22.00	\$	
Independent Claims	5 - 3 =	2	x \$82.00	\$164.00	
Multiple dependent claims(s) (if applicable)			+ \$270.00	\$	
TOTAL OF ABOVE CALCULATIONS =				\$262.00	
Reduction by $\frac{1}{2}$ for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				\$	
				SUBTOTAL =	\$262.00
Processing fee of \$130.00 for furnishing the English translation later the <u>20</u> - 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				+ \$	
				TOTAL NATIONAL FEE =	\$262.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				+ \$	
				TOTAL FEES ENCLOSED =	\$262.00
				Amount to be:	
				refunded	\$
				charged	\$

- a. A check in the amount of \$ 262.00, to cover the above fee is enclosed.
- b. Please charge my Deposit Account No. 23-3050 in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-3050. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Paul K. Legaard
 Woodcock Washburn Kurtz
 Mackiewicz & Norris LLP
 One Liberty Place - 46th Floor
 Philadelphia, PA 19103
 (215) 568-3100

SIGNATURE

Paul K. Legaard

NAME

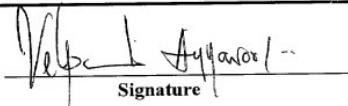
38,534

REGISTRATION NUMBER

Address all telephone calls and correspondence to:

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Philadelphia PA 19103
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Facsimile No.: (215) 568-3439

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name: <u>Velpandi AYYAVOO</u>	 Signature
Mailing Address: <u>3410 Stonecliffe Drive</u> <u>Monroeville, PA 15146 PA</u> USA	Date of Signature: <u>9/6/00</u>
City/State of Actual Residence: <u>Monroeville, Pennsylvania</u>	Citizenship: <u>India</u>

Name: <u>Thanadavarayan</u> <u>NAGASHUNMUGAM</u>	 Signature
Mailing Address: <u>3410 Stonecliffe Drive</u> <u>Monroeville, PA 15146 PA</u> USA	Date of Signature: <u>Sep 06 2000</u>
City/State of Actual Residence: <u>Havertown, Pennsylvania</u>	Citizenship: <u>India</u>

Name: <u>David B. WEINER</u>	<u>David W.</u> Signature
Mailing Address: <u>717 Beacom Lane</u> <u>Merion Station, PA</u> 19066 <i>PA</i>	Date of Signature: <u>9/11/00</u>
City/State of Actual Residence: <u>Merion Station, Pennsylvania</u>	Citizenship: <u>United States</u>

SEQUENCE LISTING

<110> Ayyavoo, Velpandi
Nagashunmugam, Thandavarayan
Weiner, David B.
University of Pennsylvania

<120> ATTENUATED VIF DNA IMMUNIZATION CASSETTES FOR GENETIC
VACCINES

<130> UPAP-0263

<140> HEREWITH

<141> 1998-09-18

<160> 46

<170> PatentIn Ver. 2.0

<210> 1

<211> 190

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

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Arg Ile Arg Thr Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Arg Trp Phe Tyr Arg His His Tyr Glu Ser Pro His Pro
35 40 45

Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu Glu
50 55 60

Thr Thr Thr Tyr Trp Gly Leu His Gly Glu Arg Asp Trp His Leu Gly
65 70 75 80

Gln Gly Val Ser Ile Glu Trp Arg Arg Lys Arg Tyr Ser Thr Gln Val
85 90 95

Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe Asp Cys
100 105 110

Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg Val Ser
115 120 125

Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser Leu Gln
130 135 140

Tyr Leu Ala Leu Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys Pro Pro
145 150 155 160

Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys Pro Gln
165 170 175

Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 2

<211> 26

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Novel Sequence

<400> 2

gaaagcttat ggaaaacaga tggcag 26

<210> 3

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 3

gcaaagcttt cattgtatgg ctc 23

<210> 4

<211> 190

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 4

Met	Glu	Asn	Arg	Trp	Gln	Val	Ile	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10				15				

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Ser	Lys
	20				25				30						

Lys	Ala	Arg	Glu	Trp	Phe	Tyr	His	His	Tyr	Gln	Ser	Pro	His	Pro	Lys
	35				40				45						

Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu	Glu	Ile
	50				55				60						

Thr	Ser	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His	Leu	Gly
	65				70			75				80			

Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr	His	Val
	85					90				95					

Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe	Asp	Cys
	100					105			110						

Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg	Val	Ser
	115				120				125						

Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser	Leu	Gln
	130				135			140							

Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	Pro	Pro
	145				150			155				160			

Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys	Pro	Gln
	165					170				175					

Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His		
	180				185				190						

<210> 5

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 5

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
I					5				10					15	

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
							20		25			30			

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
						35		40			45				

Pro	Arg	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
						50		55			60				

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
						65		70			75		80		

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
						85			90			95			

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
						100		105			110				

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
						130		135			140				

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
							145		150			155		160	

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 6

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 6

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10					15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
	35					40				45					

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50				55				60						

Glu	Thr	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65				70			75		80					

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85					90				95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105			110							

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
		115				120			125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130				135			140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Pro	Ser	Vai	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
		165				170				175					

Pro	Gin	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
		180				185			190						

<210> 7

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 7

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1					5			10				15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Thr	Tyr	His	Met	Tyr	Arg	Ser
	20						25				30				

Gln	Lys	Ala	Arg	Glu	Trp	Phe	Asn	Arg	His	His	Tyr	His	Ser	Pro	His
	35					40				45					

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50				55				60						

Ala	Ile	Pro	Thr	Phe	Trp	Gly	Leu	His	Thr	Gly	Glu	Asp	Trp	His
	65				70			75			80			

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85					90				95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105			110							

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130				135			140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155			160				

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170			175				

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 8

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 8

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5					10						15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
20					25						30				

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
35				40					45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
50				55				60							

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
65				70				75				80			

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
85					90				95						

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	His	Leu	Ile	His	Leu	Cys	Tyr	Phe
100				105					110						

Asp	Cys	Leu	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
115				120					125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
130				135				140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145				150				155			160				

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
165					170				175						

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
180				185					190						

<210> 9

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 9

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10				15				

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
	20				25				30						

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
	35				40				45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
	50				55			60							

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
	65				70			75		80					

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90				95						

His	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
	115				120				125						

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
	130				135			140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
		165				170				175					

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
		180			185				190						

<210> 10

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 10

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
20							25					30			

Lys	Lys	Ala	Arg	Glu	Trp	Phe	Tyr	Arg	His	His	Tyr	Gln	Ser	Pro	His
35						40					45				

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Glu	Asp	Ala	Arg	Leu
50						55				60					

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Thr	Gly	Glu	Arg	Asp	Trp	His
65						70				75			80		

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
						85				90			95		

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	His	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100					105				110					

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115			120			125			

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
						130			135			140			

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
							145		150		155			160	

Pro	Pro	Leu	Ala	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180			185			190			

<210> 11
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 11
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Tyr Arg His His Tyr Gln Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Val Ile Thr Thr Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 12
<211> 192
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 12
Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Thr Trp Asn Ser Leu Val Lys Tyr His Met Tyr Arg Ser
20 25 30

Lys Lys Ala Arg Glu Trp Phe Asn Arg His His Tyr His Arg Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Glu Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Phe Trp Gly Leu His Thr Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly His Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Arg Ala Gly His Ser Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Ile Ala Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 13

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 13

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	Tyr	His	Met	Tyr	Arg	Ser
20					25						30				

Gln	Lys	Glu	Arg	Glu	Trp	Phe	Asn	Arg	His	His	Tyr	His	Ser	Pro	His
35						40					45				

Pro	Glu	Gln	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Val	Asp	Gly	Arg	Leu
50					55				60						

Glu	Lys	Ile	Ala	Val	Trp	Ser	Leu	Asp	Thr	Gly	Glu	Gly	Val	Trp	His
65				70				75					80		

Arg	Gly	His	Arg	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
85						90					95				

Gin	Val	Asp	Pro	Asp	Leu	Val	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
100					105			110							

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	His	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Arg	Ala	Gly	His	Ser	Lys	Val	Gly	Ser
130				135				140							

Leu	Gln	Tyr	Leu	Ala	Ile	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
145					150				155			160			

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165				170			175			

Pro	Gin	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 14

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 14

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Arg	Ile	Arg	Thr	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20						25					30			

Lys	Lys	Ala	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40						45			

Pro	Lys	Val	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Gly	Asp	Gly	Arg	Leu
	50				55						60				

Glu	Lys	Thr	Ala	Val	Trp	Ser	Leu	Gln	Ala	Gly	Asp	Gly	Val	Trp	His
	65				70					75				80	

Arg	Gly	His	Pro	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85						90					95			

Gln	Val	Asp	Pro	Asp	Leu	Val	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105						110				

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
		115				120					125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130				135					140					

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150					155				160	

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
		165				170						175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
		180			185						190				

<210> 15

<211> 191

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 15

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1				5			10					15			

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20				25					30					

Lys	Lys	Ala	Arg	Thr	Trp	Phe	Ser	Arg	His	His	Tyr	Gly	Ser	Pro	His
	35					40					45				

Pro	Lys	Val	Cys	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55			60							

Val	Ile	Thr	Thr	Tyr	Trp	Ser	Leu	His	Ala	Gly	Glu	Asp	Trp	His	Val
65				70				75				80			

Gly	Gln	Arg	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr	Gln
	85					90					95				

Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe	Asp
	100				105				110						

Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg	Val
	115				120					125					

Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser	Leu
	130				135				140						

Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	Pro
145					150				155			160			

Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys	Pro
	165				170					175					

Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His	
	180				185					190					

<210> 16

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 16

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Thr	Tyr	Phe	Ser
	20				25					30					

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40				45						

Pro	Asn	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55			60							

Val	Thr	Thr	Pro	Tyr	Trp	Gly	Leu	His	Gly	Gly	Glu	Arg	Asp	Trp	Tyr
65				70			75				80				

Leu	Ala	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85					90				95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130				135				140						

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	
145					150			155			160				

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165			170			175				

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185			190				

<210> 17

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met	Glu	Asn	Arg	Trp	Glu	Val	Met	Ile	Val	Trp	Glu	Val	Asp	Arg	Met
1	5				10						15				

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20				25				30						

Lys	Lys	Ala	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40				45					

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55				60						

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
	65				70				75			80			

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85						90			95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
							130		135		140				

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
					145			150		155		160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
						165			170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
							180		185			190			

<210> 18

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 17

Met	Glu	Asn	Arg	Trp	Gin	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20						25					30			

Lys	Asn	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Asp	Ser	Pro	His
	35					40					45				

Pro	Val	Gln	Ser	Ser	Thr	Ala	His	Ile	Pro	Leu	Gly	Asp	Gly	Arg	Leu
	50					55					60				

Gln	Lys	Ile	Ala	Phe	Trp	Ser	Leu	Asp	Ala	Gly	Glu	Arg	Asp	Trp	His
	65					70				75				80	

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85						90					95			

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100						105					110			

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
							115				120			125	

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
							130			135		140			

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145						150				155		160		

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
							165			170			175		

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Arg	His	Thr	Met	Asn	Gly	His
							180			185			190		

<210> 19

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 19

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Tyr Arg His His Tyr Asp Ser Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Thr Thr Thr Tyr Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Gly Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

His Val Asp Pro Asp Leu Ala Asp Gln Leu Ile His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly His Arg Gly Ser His Thr Met Asn Gly His
180 185 190

<210> 20

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 20

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1	5						10					15			

Thr	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser
	20				25					30					

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35					40				45					

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50					55			60						

Val	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
	65				70				75			80			

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85						90			95					

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Thr	His	Leu	Tyr	Tyr	Phe
	100				105				110						

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
						115		120			125				

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
						130		135		140					

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	
	145				150				155		160				

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
					165				170			175			

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
						180		185		190					

<210> 21
<211> 188
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 21

Met Glu Asn Arg Trp Gln Val Met Ile Val Trp Gln Val Asp Arg Met
1 5 10 15

Arg Ile Arg Ala Trp Asn Ser Leu Val Lys His His Met Tyr Val Ser
20 25 30

Lys Lys Ala Lys Lys Trp Phe Asn Arg His His Tyr Asp Arg Pro His
35 40 45

Pro Lys Val Ser Ser Glu Val His Ile Pro Leu Gly Asp Ala Arg Leu
50 55 60

Glu Ile Thr Thr Phe Trp Gly Leu His Ala Gly Glu Arg Asp Trp His
65 70 75 80

Leu Gly Gln Arg Val Ser Ile Glu Trp Arg Lys Arg Arg Tyr Ser Thr
85 90 95

Gln Val Asp Pro Asp Leu Ala Asp Gln Leu Thr His Leu Tyr Tyr Phe
100 105 110

Asp Cys Phe Ser Glu Ser Ala Ile Arg Lys Ala Ile Leu Gly Tyr Arg
115 120 125

Val Ser Pro Arg Cys Glu Tyr Gln Ala Gly His Asn Lys Val Gly Ser
130 135 140

Leu Gln Tyr Leu Ala Leu Ala Leu Ile Thr Pro Lys Lys Ile Lys
145 150 155 160

Pro Pro Leu Pro Ser Val Arg Lys Leu Thr Glu Asp Arg Trp Asn Lys
165 170 175

Pro Gln Lys Thr Lys Gly Thr Glu Gly Ala Ile Gln
180 185

<210> 22

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 22

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met
1		5		10		15									

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Phe	Val	Ser
	20				25				30						

Lys	Lys	Ala	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His
	35				40			45						

Pro	Lys	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu
	50				55			60							

Glu	Ile	Thr	Thr	Phe	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His
	65			70			75		80						

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr
	85				90				95						

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe
	100				105			110							

Gly	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg
	115				120			125							

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser
	130			135				140							

Leu	Gln	Tyr	Leu	Gly	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys
	145				150			155		160					

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys
	165					170				175					

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His
	180				185			190							

<210> 23

<211> 192

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 23

Met	Glu	Asn	Arg	Trp	Gln	Val	Met	Ile	Val	Trp	Gln	Val	Asp	Arg	Met	
1																15

Arg	Ile	Arg	Ala	Trp	Asn	Ser	Leu	Val	Lys	His	His	Met	Tyr	Val	Ser	
																20
																25
																30

Lys	Lys	Ala	Lys	Lys	Trp	Phe	Tyr	Arg	His	His	Tyr	Glu	Ser	Pro	His	
																35
																40
																45

Pro	Gln	Val	Ser	Ser	Glu	Val	His	Ile	Pro	Leu	Gly	Asp	Ala	Arg	Leu	
																50
																55
																60

Glu	Ile	Thr	Thr	Tyr	Trp	Gly	Leu	His	Ala	Gly	Glu	Arg	Asp	Trp	His	
																65
																70
																75
																80

Leu	Gly	Gln	Gly	Val	Ser	Ile	Glu	Trp	Arg	Lys	Arg	Arg	Tyr	Ser	Thr	
																85
																90
																95

Gln	Val	Asp	Pro	Asp	Leu	Ala	Asp	Gln	Leu	Ile	His	Leu	Tyr	Tyr	Phe	
																100
																105
																110

Asp	Cys	Phe	Ser	Glu	Ser	Ala	Ile	Arg	Lys	Ala	Ile	Leu	Gly	Tyr	Arg	
																115
																120
																125

Val	Ser	Pro	Arg	Cys	Glu	Tyr	Gln	Ala	Gly	His	Asn	Lys	Val	Gly	Ser	
																130
																135
																140

Leu	Gln	Tyr	Leu	Ala	Leu	Ala	Ala	Leu	Ile	Thr	Pro	Lys	Lys	Ile	Lys	
																145
																150
																155
																160

Pro	Pro	Leu	Pro	Ser	Val	Arg	Lys	Leu	Thr	Glu	Asp	Arg	Trp	Asn	Lys	
																165
																170
																175

Pro	Gln	Lys	Thr	Lys	Gly	His	Arg	Gly	Ser	His	Thr	Met	Asn	Gly	His	
																180
																185
																190

<210> 24

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 24

Ile Glu Trp Arg Lys Lys Arg Tyr
1 5

<210> 25

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 25

Asp Arg Trp Asn Lys Pro Gln
1 5

<210> 26

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 26

Ser Leu Gln Tyr Leu Ala
1 5

<210> 27

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 27

atggaaaaca gatggcagggt gattattgtg tggcaggtag acaggatgag gattagaaca 60
 tggacagt tagtaaaata ccatatgtat tgatcaaaga aagctaggaa atggtttat 120
 tgacatcaact atcaaaggcc tcataccaaa gtaagtctcg aagtacacat cccactagag 180
 gatcttagat tggaaataac atcatttgg ggctgcata caggagaaag agactggcat 240
 tgggtcagg gagtctccat agaatggagg aaaaggagat atagcacaca cgtcgaccct 300
 gatctagcag accaactaat tcatactgtat tattttgatt gttttcaga atctgcata 360
 agaaaagcca tattaggaca cagagttgti cttaggtgt aatatcgacg aggacatagc 420
 aaggttagat cactacgat ctggcaata cgacgatcaa taacaccaa aaagataaag 480
 ccacccitgc cgagtgtcg gaaatgaca gaggatagat ggaacaagcc ccagaagacc 540
 aaggccaca gaggagcca tacaatgtaa ggacactag 579

<210> 28

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 28

atggaaaaca gatggcagggt gatgtttgtg tggcaggtag acaggatgag gattagaaca 60
 tggacagt tagtaaaata ccatatgtat agatcaaaga aagctaggaa atggtttat 120
 agacatcaact atcaaaggcc tcataccaaa gtaagtctcg aagtacacat cccactagag 180
 gatcttagat tggaaataac aacatattgg ggctgcata caggagaaag agactggcat 240
 tgggtcagg gagtctccat agaatggagg aaaaggagat atagcacaca atgagaccc 300
 gatctagcag accaactaat tcatactgtat tattttgatt gttttcaga atctgcata 360
 agaaaagcca tattaggaca cagagttgti cttaggtgt aatatcgacg aggacatagc 420
 aaggttagat cactacgat ctggcaata cgacgatcaa taacaccaa aaagataaag 480
 ccacccitgc cgagtgtcg gaaatgaca gaggatagat ggaacaagcc ccagaagacc 540
 aaggccaca gaggagcca tacaatgtaa ggacactag 579

<210> 29

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 29

atggaaaaca gatggcagggt gatgtttgtg tggcaggtag acaggatgag gattagaaca 60
 tggacagt tagtaaaata ccatatgtat agatcaaaga aagctaggaa atggtttat 120
 agacatcaact atcaaaggcc tcataccaaa gtaagtctcg aagtacacat cccactagag 180
 gatcttagat tggaaataac aacatattgg ggctgcata caggagaaag agactggcat 240
 tgggtcagg gagtctccat agaatggagg aaaaggagat atagcacaca atgagaccc 300

gatcttagcag accaactaat tcacitgtat tattttgtt gttttcaga atctgcata 360
 agaaaagcca tattaggaca cagagttgtt cctagggttg aatatcgacc aggacatagc 420
 aaggttaggt caactacgat ctggcaata gcacgatcaa taacacccaa aaagataaaag 480
 ccacccatgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
 aagggccaca gagggagcca tacaatgaat ggacactag 579

<210> 30

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 30

atggaaaaca gatggcagggt gatgttttgtt tggcaggtag acaggatgag gattagaaca 60
 tggAACAGTT tagtaacata ccatatgtat agatcacaga aagcttaggga atggtttat 120
 agacatcaatc acatcagtc tcatccaaaaa gtaagtccg aagtccacat cccactagag 180
 gatgctagat tggcaataacc aacatttgg ggctcgtca caggagaaag agactggcat 240
 tgggttcagg gatgttcat agaaatggggg aaaaggatgat atagcacaca atgatgaccc 300
 gatcttagcag accaactaat tcacitgtat tattttgtt gttttcaga atctgcata 360
 agaaaagcca tattaggaca cagagttgtt cctagggttg aatatcgacc aggacatagc 420
 aaggttaggt caactacgat ctggcaata gcacgatcaa taacacccaa aaagataaaag 480
 ccacccatgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
 aagggccaca gagggagcca tacaatgaat ggacactag 579

<210> 31

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 31

atggaaaaca gatggcagggt gatgttttgtt tggcaggtag acaggatgag gattagaaca 60
 tggAACAGTT tagtaaaataa ccatatgtat agatcaaaga aagcttaggga atggtttat 120
 agacatcaatc acatcagtc tcatccaaaaa gtaagtccg aagtccacat cccactagag 180
 gatgctagat tggaaataac aacatattgg ggctcgtca caggagaaag agactggcat 240
 tgggttcagg gatgttcat agaaatggggg aaaaggatgat atagcacaca cgfcgaccc 300
 gatctcgccag accaccaata tcacitgtt tattttgtt gttttcaga atctgcata 360
 agaaaagcca tattaggaca cagagttgtt cctagggttg aatatcgacc aggacatagc 420
 aaggttaggt caactacgat ctggcaata gcacgatcaa taacacccaa aaagataaaag 480
 ccacccatgc cgagtgtcag gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
 aagggccaca gagggagcca tacaatgaat ggacactag 579

<210> 32

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 32

atggaaaaca gatggcaggt gatgattgtg tggcaggtag acaggatgag gattagaaca 60
tggAACAGTT tagtaaaaata ccataatgtat agatcaaAGGA aagctAGGGG atggTTTtat 120
agacatcaCTCt atccaaAGTC tcataccaaa gtaagtTCAG aagtacacat cccactAGAG 180
gatgCTGATAG tggtaataAC aacataATGG ggTCGCTA caggAGAAAG agactGGCAT 240
ttgggtcagg gagTCCTCAT aagaATGGGGG aaaAGGAGAT atagcacaca ctgacacCCt 300
gatCTAGCAG accAACTAAT tcACtGTAT tattttGATT gttttcAGA atCTGCTATA 360
agAAAAGCCA tattAGGACA cAGGTTAGT CCTAGGTGt aATATCGAGC aggACATAGC 420
aaggTAGGAT cactACAGTA CTGGCAATA GcAGCATTAA taACACCAAA aaAGATAAAG 480
ccACCTTGG CGAGTGTAGC gaaACTGACA gaggatAGAT ggaACAAAGCC ccAGAAAGACC 540
aaggGCCACA gaggGAGCCA tacaATGAAT ggacACTAG 579

<210> 33

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 33

atggaaaaca gatggcaggt gatgattgtg tggcaggtag acaggatgag gattagaaca 60
tggAACAGTT tagtaaaaata ccataatgtat agatcaaAGGA aagctAGGGG atggTTTtat 120
agacatcaCTCt atccaaAGTC tcataccaaa gtaagtTCAG aagtacacat cccactAGAG 180
gatgCTGATAG tggtaataAC aacataATGG ggTCGCTA caggAGAAAG agactGGCAT 240
ttgggtcagg gagTCCTCAT aagaATGGGGG aaaAGGAGAT atagcacaca ctgacacCCt 300
gatCTAGCAG accAACTAAT tcACtGTAT tattttGATT gttttcAGA atCTGCTATA 360
agAAAAGCCA tattAGGACA cAGGTTAGT CCTAGGTGt aATATCGAGC aggACATAGC 420
aaggTAGGAT cactACAGTA CTGGCAATA GcAGCATTAA taACACCAAA aaAGATAAAG 480
ccACCTTGG CGAGTGTAGC gaaACTGACA gaggatAGAT ggaACAAAGCC ccAGAAAGACC 540
aaggGCCACA gaggGAGCCA tacaATGAAT ggacACTAG 579

<210> 34

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 34

atggaaaaca gatggcaggt gatgattgtg tggcaggtag acaggatgag gattagaaca 60
tggAACAGT tagtaaaata ccatatgtat agatcaaaga aagctaggga atggtttat 120
agacatcaact atcaaAGTC tcatccaaaa gtaagtTCAG aagtacacat cccactagag 180
gtatGCTAGAT tggtaataac aacattttgg ggTCGcata caggagaAG agactGGCAT 240
ttggcagg gagtCTCcat agaaTgggg AAAAGGAGAT atAGCACACa CGTAGACCCt 300
gatCTAGCAG accaactaa tcatCTGtAT tattttGAT GTTTTCAGA ATCTGCTATA 360
agaaaAGCCA tattAGGACA CAGAGTGTG CCTAGGTGt aatatCGAGC AGGCACATAGC 420
aaggtaggat caTACAGTA CTGGCA TA GCAGCATTA ACACCAAA AAAGATAAG 480
CCACCTTtGC CGAGTGTcAG gaaACTGACA GAGGATAGAT ggaACAAgCc CCAGAAGACC 540
aaggGTCACA gaggGAGGCCa TACAATGAAT ggACACTAG 579

<210> 35

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 35

atggaaaaca gatggcaggt gatgattgtg tggcaggtag acaggatgag gattagaaca 60
tggAACAGT tagtaaaata ccatatgtat agatcaaaga aagctaggga atggtttat 120
agacatcaact atcacCGTC tcatccaaaa gtaagtTCAG aagtccacat cccactagag 180
gtatGCTAGAT tggAAATAAC aacattttgg ggTCGcata caggagaAG agactGGCAT 240
ttggcagg gagtCTCcat agaaTgggg AAAAGGAGAT atAGCACACa CGTAGACCCt 300
gatCTAGCAG accaactaa tcatCTGtAT tattttGAT GTTTTCAGA ATCTGCTATA 360
agaaaAGCCA tattAGGACA CAGAGTGTG CCTAGGTGt aatatCGAGC AGGCACATAGC 420
aaggtaggat caTACAGTA CTGGCA TA GCAGCATTA ACACCAAA AAAGATAAG 480
CCACCTTtGC CGAGTGTcAG gaaACTGACA GAGGATAGAT ggaACAAgCc CCAGAAGACC 540
aaggGTCACA gaggGAGGCCa TACAATGAAT ggACACTAG 579

<210> 36

<211> 584

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 36

atggaaaaca gatggcaggt gatgattgtg tggcaggtag acaggatgag gattagaaca 60

tggAACAGT tagAAATAA ccATATGT tgCTAAAGA aaAGAAAGAA aggGAATGGT 120
 ttTAAGACA tcACtATCAG acGCCCTCATC cAGAAcAAAGA ttCAACAGCC cacATCCGC 180
 tagTGATGG tagATGGAA aaaATAGCAG ttGGAGGT ggATACAGGG gtATGGCGTC 240
 ggcACAGGGC gcATCAGTC tcCATAGAA ggAGAAAGG gagATATGAC acACAATGAG 300
 acCTGATCt agTAGACCAA ctaATTCAT tgTTATTt tgATGTTt tcAGATCTG 360
 ctTAAGAAA agCCATATAA ggCACACAGAG ttAGTCCTAG gtGTGAATAT cgAGCAGGAC 420
 atAGCAAGGT aggATCAGTC cAGTCTGG caATAGCAG tcATTAACAA cAAAGAAAGA 480
 TAAGGCACC ttGCAGCGT gtCAGGAAAC tgCAAGAGGAG tagATGGAC aAGCCCCAA 540
 agACCAAGGG ccACAGGGG aggACCATAC tGAATGACAA ctAG 584

<210> 37

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 37

<210> 38

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Des

<400> 38

tggaacagt

agaaaaggcca tattaggata tagatgtgt ccttaggtgt aatccaaagc aggacataat 420
aggtaggt ctctacgta ctggcaacta ggcacatcaa taacacccaa gaagataaa 480
ccatctttt ctatgtgt gaaacgtaca gaggatataat ggaacaaggcc ccagaaggacc 540
aggccca gaggaggcca tacaatgtat ggcacatgt 579

<210> 39

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 39

<210> 40

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 40

<210> 41
<211> 579
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 41
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tggAACAGTT tagtaaaaca ccatagttat gtttCAAAGA acgtctaagaat atggTTTAT 120
cgacatcaat atgcacGCC tcataccAGTC caaaGTCaa cAGCCACAT cccGCTAGGG 180
gatGCTGATG tgcaGAAAAT aGACTTTGg agtCTGATG cAGGAGAAAG agactGGCAT 240
ttggGTcagg gagtCTCcat aGAAATGGGG AAAAGGGAGAT atAGCACACA aGTAgaCCt 300
gaccTGGCAG accaACTAAT tcataCTGAT tATTTGATt GTTTTCAGA atCTGCTATA 360
agaaaAGCCA tattAGGATA tagAGTGTG ctTAGGTGTG aataCCAAAG aggACATAAT 420
aaggTAGGAT ctCTACAGTA ctTGGCACTA GcAGCATAA TAACACCAAa GAAGATAAAG 480
ccACCTTGc CTAGTGTGAG gaACTGACa GAGGATAGAT gGAACAAGCC CcAGAAAGACC 540
aaggGCCACa gAGGGAGGCC TACAATGATt GGACACTAG 579

<210> 42
<211> 579
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Novel Sequence

<400> 42
atggaaaaca gatggcaggat gatgattgtg tggcaagtag acaggatgag gattagagca 60
tggAACAGTT tagtaaaaca ccatagttat gtttCAAAGA acgtctaagaat atggTTTAT 120
agacatcaat atgcacGCC tcataccAGTC caaaGTCaa cAGCCACAT cccGCTAGGG 180
gatGCTGATG tgcaGAAAAT aGACTTTGg agtCTGATG cAGGAGAAAG agactGGCAT 240
ttggGTcagg gagtCTCcat aGAAATGGGG AAAAGGGAGAT atAGCACACA cTAGACACt 300
gaccTGGCAG accaACTAAT tcataCTGAT tATTTGATt GTTTTCAGA atCTGCTATA 360
agaaaAGCCA tattAGGATA tagAGTGTG ctTAGGTGTG aataCCAAAG aggACATAAT 420
aaggTAGGAT ctCTACAGTA ctTGGCACTA GcAGCATAA TAACACCAAa GAAGATAAAG 480
ccACCTTGc CTAGTGTGAG gaACTGACa GAGGATAGAT gGAACAAGCC CcAGAAAGACC 540
aaggGCCACa gAGGGAGGCC TACAATGATt GGACACTAG 579

<210> 43
<211> 579
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 43

atggaaaaca gatggcaggt gatgatttgt tggcaagtag acaggatgac gattagagca 60
tggAACAGT tagtaaaaca ccatatgtat gttcaaga aagctaagaa atggTTAT 120
agacatcact atgaaagccc tcataccaaa gtaagtTCAG aagtacacat cccactAGGG 180
gatgCTAGAT tggtGATAAC aacatATTGG ggTCGcatG caggAGAAAG agactGGCAT 240
ttggGTcAGG gagTCCTCAT agaaTGGGG AAAAGGAGAT atAGCACACA atgAGACCT 300
gactTGGCAG accaACTAAC tcATCtgTA TATTTGATT gttttcAGA atCTGCTATA 579

<210> 44

<211> 578

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 44

atggaaaaca gatggcaggt gatgatttgt tggcaagtag acaggatgag gattagagca 60
tggAACAGT tagtaaaaca ccatatgtat gttcaaga aagctaagaa atggTTAT 120
agacatcact atgaccGCC tcataccaaa gtaagtTCAG aagtccacat cccactAGGG 180
gatgCTAGAT tggtGAGATAAC aacatTTGG ggTCGcatG caggAGAAAG agactGGCAT 240
ttggGTcAGCAG gagTCCTCAT agaaTGGGG AAAAGGAGAT atAGCACACA atgAGACCT 300
gactTGGCAG accaACTAAC tcATCtgTA TATTTGATT gttttcAGA atCTGCTATA 578

<210> 45

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 45

atggaaaaca gatggcaggt gatgatttgt tggcaagtag acaggatgag gattagagca 60

tggaacagtt tagtaaaaaca ccataatgtt gttcaaaaga aagctaagaa atggtttat 120
agacatcaact atgaaagccc tcatccaaaa gtaagtcag aagtacacat cccactaggg 180
gatgcctagat tgtagataac aacattttg ggtctgcattt caggagaaaag agactggcat 240
ttgggtcagg gagtctccat agaatggagg aaaaggat atagcacaca agtagaccc 300
gacctggcag accaactaat tcacatgtat tatttttgtt gtttticaga atctgcata 360
agaaaagcca tattaggata tagatgtat ctctagggtg aataccaaagc aggacataat 420
aaggtagat ctctacagta ctggcacta gcacattttaa taacacccaa gaagataaag 480
ccaccccttgc ctatgtgtgaa gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggggccaca gaggggagcca tacaatgaat ggacactag 579

<210> 46

<211> 579

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Novel Sequence

<400> 46

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tggaacagt tagtaaaaaca ccataatgtt gttcaaaaga aagctaagaa atggtttat 120
agacatcaact atgaaagccc tcatccaaaa gtaagtcag aagtacacat cccactaggg 180
gatgcctagat tgtagataac aacatatttg ggtctgcattt caggagaaaag agactggcat 240
ttgggtcagg gagtctccat agaatggagg aaaaggat atagcacaca agtagaccc 300
gacctggcag accaactaat tcacatgtat tatttttgtt gtttticaga atctgcata 360
agaaaagcca tattaggata tagatgtat ctctagggtg aataccaaagc aggacataat 420
aaggtagat ctctacagta ctggcacta gcacattttaa taacacccaa gaagataaag 480
ccaccccttgc ctatgtgtgaa gaaactgaca gaggatagat ggaacaagcc ccagaagacc 540
aaggggccaca gaggggagcca tacaatgaat ggacactag 579